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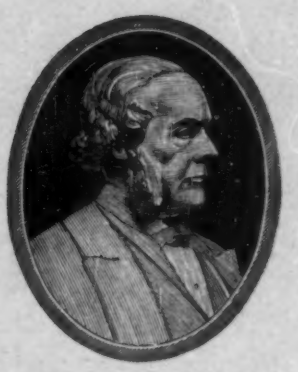

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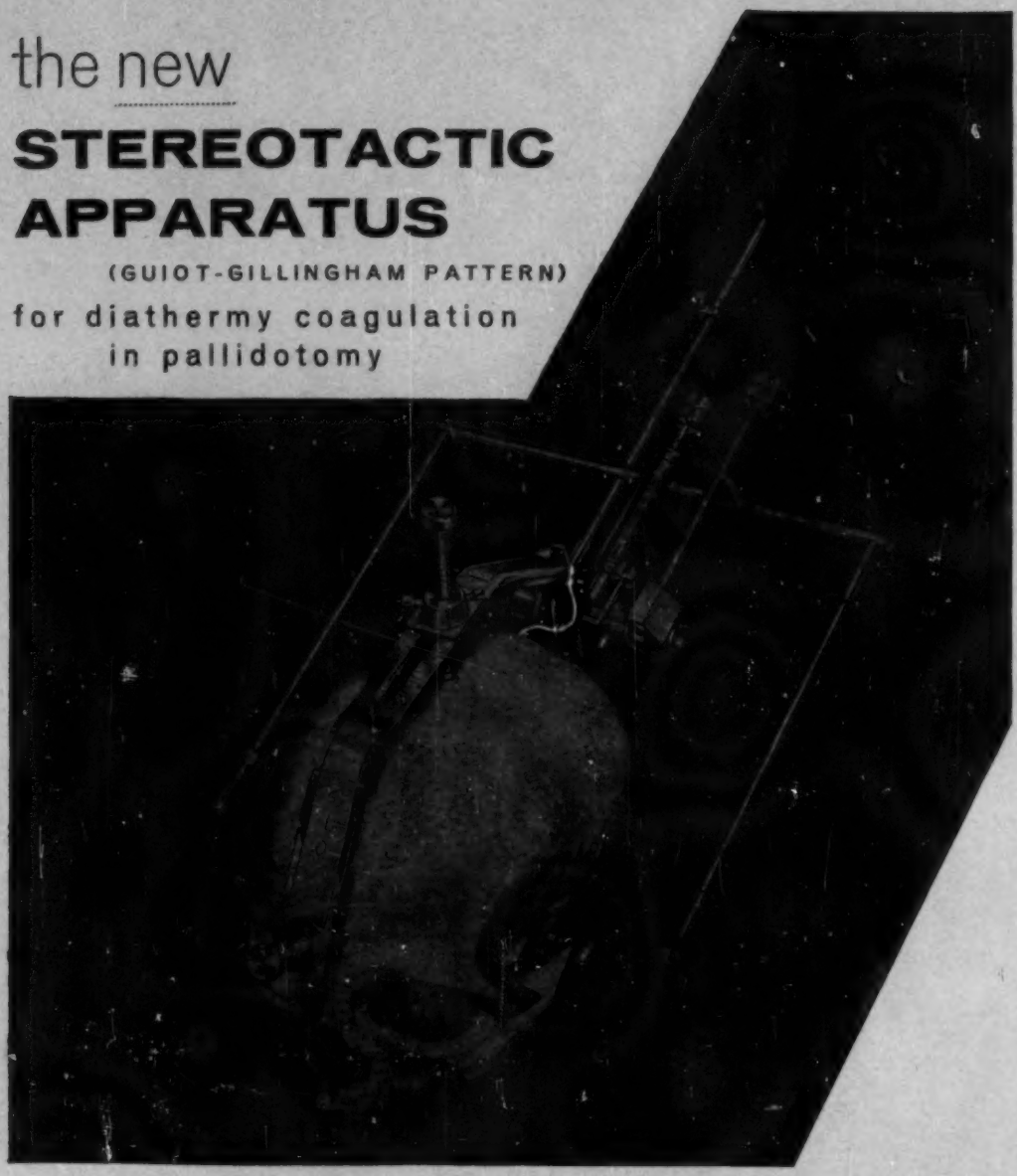

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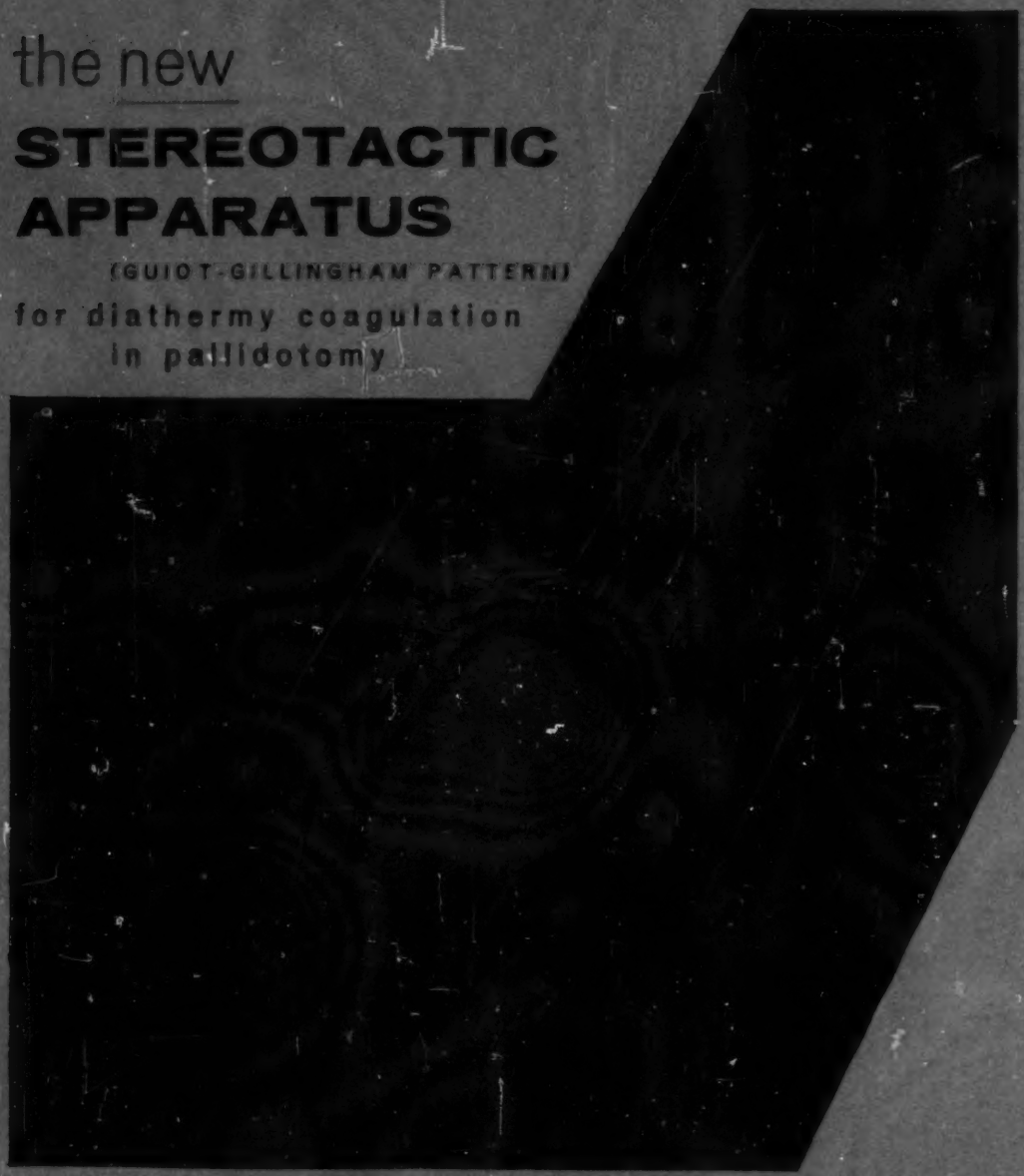

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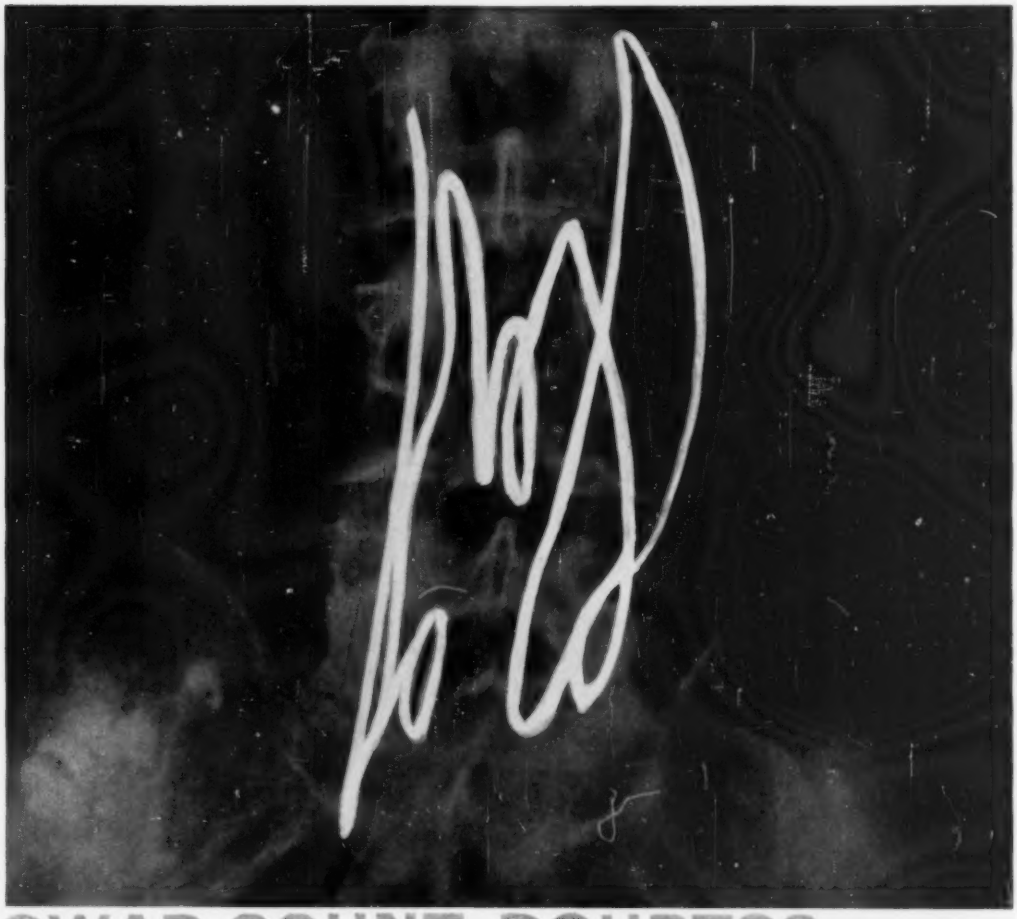

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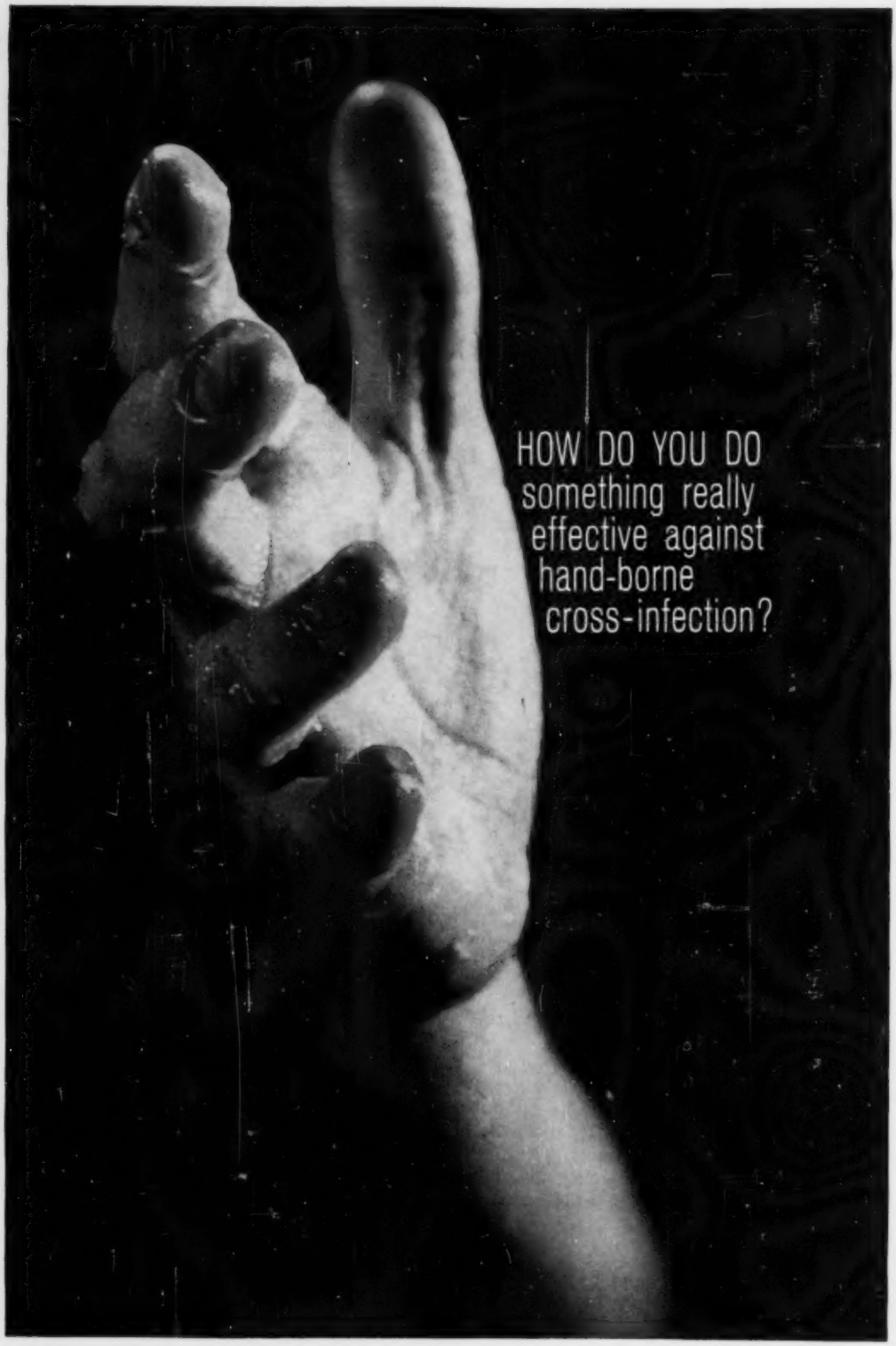
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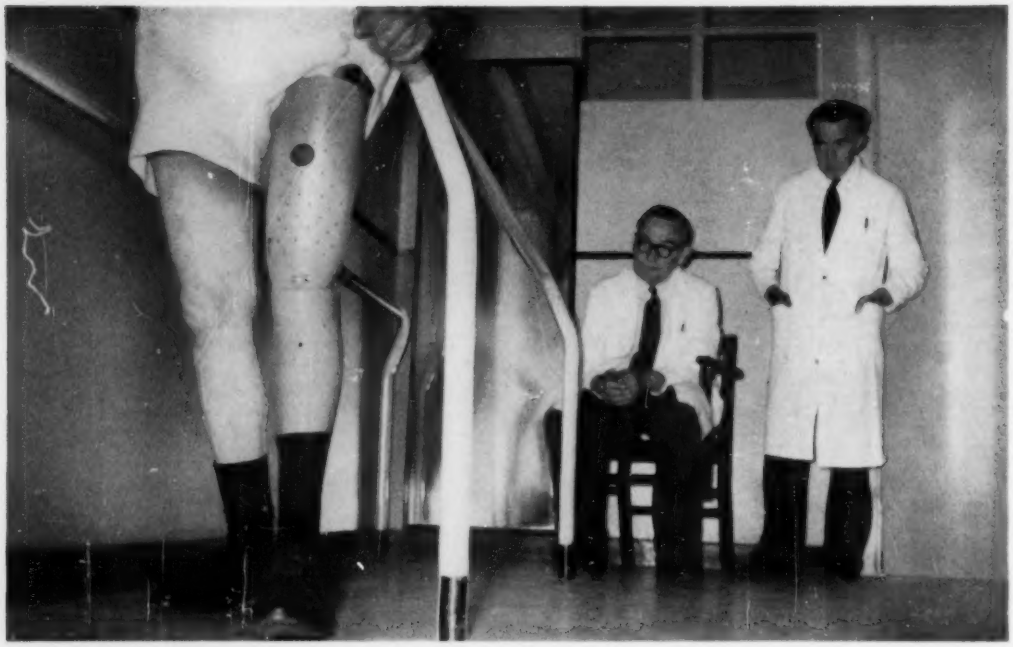

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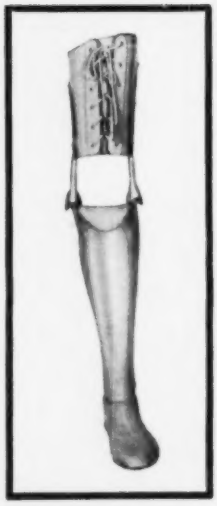

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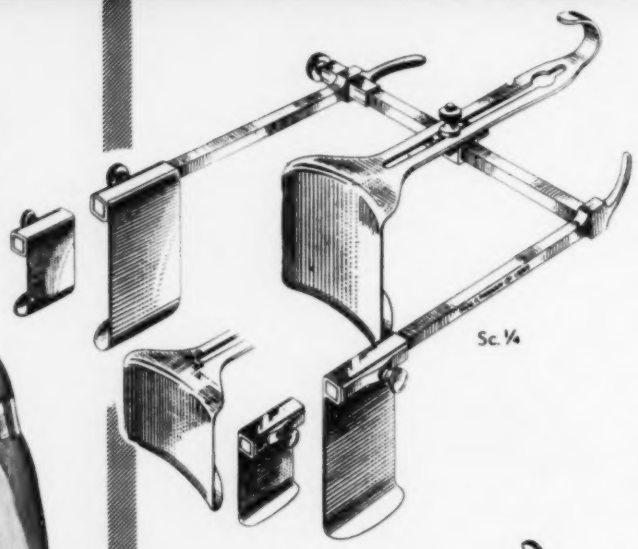

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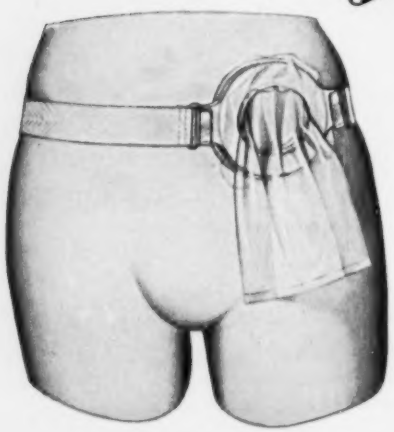

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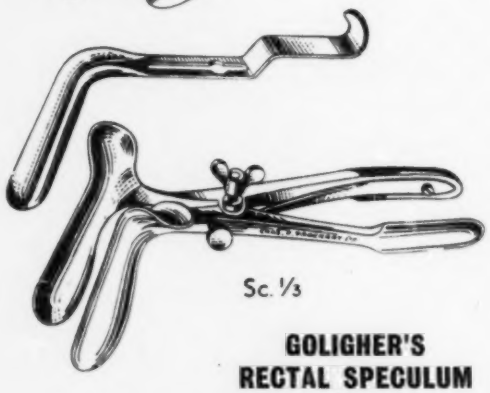

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Vide: "*The Lancet*", April 19th, 1958, pages 831-832.

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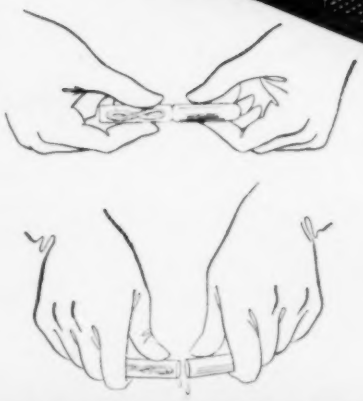

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THE
BRITISH JOURNAL OF SURGERY

VOL. XLIX JULY, 1961 No. 213

In Memoriam

Julian Taylor, C.B.E., M.S., F.R.C.S., Hon. F.R.A.C.S.

(1889–1961)

JULIAN TAYLOR died on April 15, 1961, at the age of 72. His passing leaves a sadness and yet his life was an inspiration to the countless friends, colleagues, and past students in the British Isles and the many corners of the world where his work had taken him.

He was educated at University College School and at University College, London (of which he later became a Fellow), entering University College Hospital and Medical School in 1908. He qualified in 1911 and graduated M.B., B.S. (London) with honours in Medicine in 1912. There followed house appointments at U.C.H. to Herbert Spencer, Sidney Martin, and Bilton Pollard, and in 1914 he became a Fellow of the Royal College of Surgeons.

Before the 1914 war he had joined the Territorial 3rd (London) Field Ambulance and drove horsed ambulances for fun! At the outbreak of war he was commissioned from the ranks and with his Field Ambulance (now the 85th) left for France under the command of Lt.-Col. (later Sir Thomas) Fairbank. In 1915, at the second battle of Ypres and at Loos at the end of that year, he gave with his unit much distinguished and hazardous service. In 1916 the Field Ambulance was transferred to Salonika and later Julian Taylor was in charge, successively, of the surgical divisions of the 52nd and 43rd General Hospitals in that campaign.

At the end of the war he was appointed O.B.E. and returned to U.C.H., where he proceeded to the M.S. (London) in 1920. In 1922, after some time with the newly formed Surgical Unit under Professor Choyce at U.C.H., he became Surgical Registrar to the hospital and in 1924 returned to the Unit as first assistant. In 1927 he was appointed to the Consultant staff at U.C.H. and in 1931 to the National Hospital, Queen Square, and to Harrow Hospital in 1930.

There followed in the thirties a period of advancement and consolidation in busy hospital and private practice which he conducted from his enviable house in Portland Place. At this time he had an apparently inexhaustible fund of energy to satisfy the unceasing demands of general surgery at all hours and the meticulous requirements of his neurosurgical work. Looking back it all seemed (to the onlooker) so easy and so successful; he was a master of a wide compass of surgery accomplished always with great facility and elegance. Yet now one is aware that this was but a part of his potentialities. Later events, with adversities and sorrows to come, were to show a different and indeed greater side to his character.

In 1941, when over 50, he made a personal sacrifice. Abandoning security, he rejoined the Army and was shortly appointed Consulting Surgeon,

Julian Taylor

Malaya Command. A few weeks later, at the fall of Singapore, he was made a prisoner of war. What followed in the next three and a half years it is difficult for one not present to imagine. The bare facts of Julian Taylor's incredible achievements in the Changi and Kranji prison hospitals are set out in his own lucid account in the *History of the Second World War*. His guidance and teaching of the young medical officers about him, and his training of the nursing orderlies who were caring for the sick and

wounded with such devotion, is but a small part of the tale. The manner in which he was able to produce results in his weak and emaciated patients with such slender resources is a tribute to his skill and courage and indomitable will. But more than this, there are the stories told of his constant endeavours to help in other ways. He lectured and talked on many matters; on navigation, French history, the stars, and innumerable other topics. With the assistance of two combatant officers he designed and constructed from the most unpromising materials articulating limbs for his amputees. He was proud of these and after the war was fond of demonstrating their ingenuity and artistry.

On his return at the end of 1945 he was visibly less than fit. Of his experiences he spoke little, but set about giving all possible assistance to establish those young men—not all of them doctors—who had stood by him in captivity. In 1946 he was appointed C.B.E., but his great joy at this time was his election to the Council of the Royal College, of which he remained a member until his death. He was Vice-President from 1954 to 1956.

A new phase of his varied life is now discernible and to appreciate it one must glance back at the earlier years when he came under the influence of Wilfrid Trotter at U.C.H. For Trotter he had enormous regard and affection and no doubt from him acquired many of the ways of thought and action which were to characterize his work in later years. His interest in thyroid surgery and neurological surgery stemmed from this source. These were the times when it was still possible for a surgeon of supreme ability to become a master in widely diverse fields, and Julian Taylor, like Trotter before him, was one of these. Certainly until his retirement from U.C.H. he was undertaking the most varied and heavy operating lists with the same simplicity, gentleness, and precision which had marked him out so many years before.

Until the second war he had been among the foremost of the general surgeons who undertook neurological surgery, and although he realized that a surgeon might devote all his energies to this speciality, he decided not to forgo the wider experience which he had matured. Thus after the second war he took perhaps a less prominent part in neurosurgery but continued both at Queen Square and U.C.H. to undertake the very considerable amount which came his way. It is interesting to note that although he did not publish frequently, two of his contributions to which constant reference is still made are on neurosurgical subjects. The first, on "The Invasion of the Skull by Dural Tumours", appeared in this JOURNAL in 1928, and the second, in 1934, concerned the closure of dural defects in which he described a method which is now universal practice. There is also the classic article on "Diseases of the Appendix" in *Essentials of Modern Surgery* for which countless students and young surgeons must be for ever grateful.

On returning to London in 1945 with changing circumstances he elected with quiet deliberation to devote much of his energies to teaching his undergraduates, to training young surgeons, and to the many duties which his membership of the Council of the College required of him. During these years he became President of the Sections of Surgery and of Neurology of the Royal Society of Medicine. Before the war he had been Secretary of the Association of Surgeons of Great Britain and Ireland, later serving on the Council and being elected President in 1953. He was made an Honorary F.R.A.C.S. in 1949.

Nevertheless in private work, and perhaps especially in the care of sick colleagues, the difficult problems were those upon which he was most often consulted. He gave his help unstintingly without thought of self or of the time involved. On more than one occasion he made long and tedious journeys whilst allegedly on holiday to return to the bedside where his advice was needed. His patients and friends loved and admired him for this devotion but sometimes found it difficult to know in what manner best to make acknowledgement. He seemed to need so little for himself. He had, no doubt, an outer reserve of manner, but this protected the most sympathetic and gentle of natures within. He was kind and generous to a fault and the numbers who received his help and encouragement are beyond counting.

His judgement of young people was both keen and discerning, but did not always follow general opinion. Once he was satisfied that his choice was correct he would defend these young men and women with extraordinary tenacity against the views of others, equally sincere. Occasionally events have proved him wrong, but it is true that a majority of his house surgeons have become or are becoming leaders in their chosen fields.

His old students and assistants had for him a rare affection and reverence. His bedside rounds were quiet, and his manner undemonstrative, but the substance of his thought and speech was always stimulating and provocative. Sometimes his statements seemed at first obscure, but this was a deliberate testing, to make his listeners think. His opinions, both surgical and otherwise, were firm, concise, and sound. Once given he made no concession to persons or personalities, and thereby occasionally lost some friendship but gained respect from all.

Perhaps the paragraphs above suggest too coldly Julian's personality. His was the warmest of natures, with a love of the good things of life, of entertaining and entertainment. His conversation could be full of fun and wit—often sharp and pungent, but at all times delicate. He had many interests beyond his work. For many years sailing was his main relaxation and his knowledge of our coastal waters was quite remarkable. His delight in the niceties of navigation provided a fund of amusing epics. His other hobby was his country home in Sussex, and here he kept his splendid collection of Chinese porcelain gathered over the years.

In 1926 he married Dr. Margaret Ross-Johnson and there followed a partnership in life and work which was an inspiration to those who knew them. Mrs. Taylor, who was an anæsthetist of distinction, fell ill in the early 1950's but carried on with grace and magnificent fortitude until her sad and premature death in 1955. Julian had retired from the staff of U.C.H. and the National in 1954 and this tragedy, which he had foreseen, but which he had borne with outward imperturbability, hit him hard.

A lesser man might have withdrawn to a retirement which was his due, but Julian Taylor took this as a challenge as he had earlier adversities. In 1956 he was appointed to the Chair of Surgery in the University of Khartoum and there set about with restless vigour the establishment of a training centre based on the precepts and traditions of British surgery. Through his efforts the Primary examination for the F.R.C.S. has been held there in the past two years and there are now no less than a dozen young Sudanese with their 'primary' training in England and the Sudan. He was immensely proud of these young men and spared no effort, nor himself, to assist them to success. More than this, with the help of two British surgeons whom he had personally attracted to his department, he was teaching his Sudanese undergraduates with a devotion which was only matched by the affection and regard which they had, in their turn, for him.

His whole life and energies were put at the service of the Sudanese. He made long journeys through the country to advise and operate in the various smaller centres. He established liaison with colleagues in neighbouring African countries so that an interchange of ideas might flow. He was also engaged in a programme of research into the problems of maduramycosis and stimulated the efforts of those interested in the subject in this country. He made a determined attempt by propaganda to eradicate hydatid disease in a primitive area where ignorance perpetuated it.

All this made inroads into his health and for the last two years he laboured on under great physical difficulty with calm determination. After an illness from which he appeared to make a satisfactory recovery he returned on annual leave to England in April. Two days later he died suddenly at his country home at Bepton.

Those who have had the privilege of working with him will recall best their own small segment of a life which was lived with such dignity, courage, and distinction, but, oddly perhaps, he will be most widely remembered for the magnificent example he displayed, not in England, but in Malaya and in the Sudan.

Julian Taylor is survived by his two sons.

PRIMARY HEPATIC MALIGNANCY

WITH PARTICULAR REFERENCE TO THE EMBRYOMA OF INFANCY

By J. B. M. ROBERTS

ROYAL INFIRMARY AND CHILDREN'S HOSPITAL, SHEFFIELD

RARITY has a charm and fascination which is witnessed by the numerous collectors of the uncommon in fields both beautiful and grotesque. Human pathology has for long been one of the most prolific of these fields, and there can be few surgeons who have not felt an irrational enthusiasm for some condition which has left the hidden halls of its obscurity to grace, however transiently, their experience. Whilst, however, such a condition may be granted a place of honour within the museum of a particular memory there are few of the uninitiated who can be expected to share this disproportionate interest. The reporting of the uncommon must therefore be undertaken with some definite aim other than merely to stress how Fortune has favoured one particular surgeon.

In presenting this series of cases it is hoped that some help may be given in the matters of diagnosis, treatment, and prognostication to those who have not yet experienced and considered the problem of primary malignant disease of the liver, especially in infancy.

PATHOLOGY

Primary malignant tumours of the liver have been classified into the following groups (Ackerman, 1959): (1) Liver cell carcinoma—or malignant hepatoma; (2) Adenocarcinoma of the bile-duct—or cholangioma; (3) Fibrosarcoma; (4) Hæmangio-endothelioma; (5) Leiomyosarcoma; (6) Malignant embryonal hepatoma —or embryoma. Willis (1953) has stressed, however, that differentiation into the first two groups is not absolute and states that small areas of well-differentiated columnar-celled carcinoma may on occasion be seen in liver cell tumours. Popper and Schaffner (1957) are more positive and consider the difference between the two groups too indefinite to be of value. They believe that elements of both types of change can be found in most tumours if they are examined thoroughly, but do not accept that true cholangiomata occasionally arise in the larger intrahepatic bile-ducts.

Embryoma.—Embryoma of the liver is an uncommon tumour, even relative to its rather rare carcinomatous counterpart. It consists of embryonic liver tissue sometimes accompanied by heterotopic elements such as epithelium, osteoid, and connective tissue (*Fig.* 1). Willis quotes Webster who has suggested the embryoma may represent tumour change in a primitive hepatic blastema analogous to that produced in the renal blastema by Wilms' tumour. It is distinguished from a teratoma by the absence of elements strange to the hepatic environ, such as respiratory epithelium or brain tissue.

Assessment of the incidence of these tumours is difficult but certainly few have been recorded in the literature. In a review of congenital malignant tumours Wells (1940) mentions only three which might fall into this group.

The first was that of McRae which was described as being a malignant teratoid hepatoma with osteoid tissue. Secondly came Prescott's case, described as a chiefly epithelial tumour with sarcomatous elements; this neoplasm was present in the right lobe of the liver and had ulcerated into the lumen of the stomach. Thirdly there was Nissel's case, whose clinical presentation will be discussed later. Allison and

Willis (1956) described a further case in detail and discussed the literature. They stress the rarity of the lesion, finding less than twenty recorded cases. The relationship of epithelial and mesenchymal elements in the cases reviewed was very variable and osteoid or cartilage was not invariably present. For adequate diagnosis it is apparent that the mixed nature of the

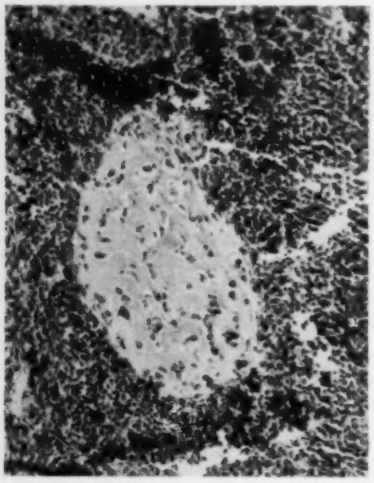

FIG. 1.—Osteogenesis within a hepatic embryoma—*Case* 2. (× 90.)

tumour must be demonstrated and that the presence of a primary source elsewhere must be excluded by a detailed autopsy. It is believed that these conditions have been fulfilled in the 3 cases to be reported.

It might be thought that the presence of calcification in these tumours would occasionally enable the radiologist to make a pre-operative diagnosis, but this is not so, for, as Tomlinson and Wolff (1942) point out, calcification may also occur in necrotic areas of carcinomata.

Metastases.—Despite the extremely vascular environment of liver tumours metastases are not as common as might be expected. Steiner (1938) in a review of 77 reported cases of primary liver carcinoma occurring in children under the age of 16 found only 22 to have evidence of metastases. In 20 of these cases deposits were found in the lungs, pleura, or pulmonary veins. He quotes Eggel, however, as finding an incidence of 66 per cent in 117 adult cases. Direct spread into the branches of the portal vein, the hepatic veins, and the inferior vena cava occurs at times and a section from the liver in *Case* 1 illustrates this vividly (*Fig.* 2).

Tendency to Bleed.—The extremely vascular environment of these tumours does, however, account for their notorious tendency to bleed. This bleeding, should it occur, may be: (1) Intraperitoneal; (2) Intrahepatic—into the bulk of the necrotic tissue; (3) Subphrenic.

1. INTRAPERITONEAL HÆMORRHAGE.—In general discussions on malignant hepatic tumours it is common to find statements that massive intraperitoneal hæmorrhage is a frequent terminal event. Nevertheless, examples are rare in the literature of Western peoples, and Rolleston and McNee (1929) were aware of such episodes only from the writings of others. Abel (1934) quotes the case described by Philip Turner where massive hæmorrhage occurred

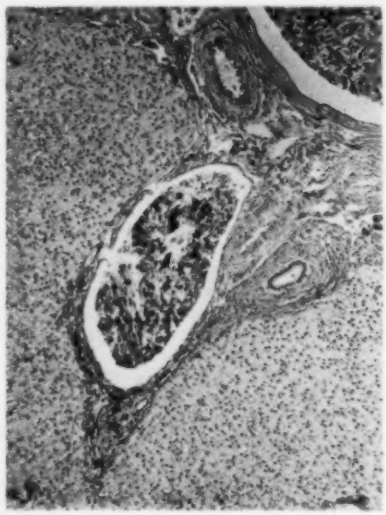

FIG. 2.—Invasion of a branch of the portal vein by the tumour in *Case* 1. (× 64.)

from a tumour which proved, however, on histological examination to be an adenoma. Specter and Chodoff (1950) reviewed a series of malignant liver tumours associated with such bleeding which they had collected from the literature and found only 11 primary tumours. In most of these cases a sudden abdominal catastrophe had been the first significant symptom. Riddell (1952) described a case of hæmoperitoneum arising from a friable white nodule, 1 cm. in diameter, present on the surface of the left lobe of the liver. The lesion was resected and proved to be a malignant hepatoma.

Ellis, Griffiths, and MacIntyre (1958) in a discussion on causes of hæmoperitoneum include the case of a man of 68 in whom the bleeding had originated from a large tumour in the right lobe of the liver. This was found on microscopic examination to be a primary carcinoma of the liver. Ewing (1940) mentions death from massive hæmorrhage due to necrosis of a liver cell carcinoma in an old man.

In infancy this complication appears to be even rarer than it is amongst adults. Steiner does not mention it. Ladd and Gross (1941) found no instance of it in the records of the Boston Children's Hospital. Nissel (1926) seems to have been the first to describe such a case. This was an infant who died shortly after birth and was found at autopsy to have a hæmoperitoneum due to the rupture of a large hepatic tumour. The pathology of this tumour has been mentioned in the discussion on embryomata.

The complication of hæmoperitoneum is well illustrated by the first case in this series.

Case 1.—Jean H., aged 2½ years. A lively little girl who had spent the day playing in the garden. Whilst being undressed in preparation for bed it was noticed that she was pale, cold, and sweating. She then held her hand over her abdomen and complained of pain. Being placed on a couch she lay there quietly; drowsy but easily roused and rational. Several times she asked for a drink. During this period she twice vomited her recently taken meal. Her bowels were opened twice, the second motion

FIG. 3.—A sketch of the operative findings in *Case* 1.

being loose and offensive but containing no blood. She was admitted to the Sheffield Children's Hospital and when examined she was still complaining of pain and her drowsiness was apparent. Despite her extreme pallor her respiration was quiet and not excessively rapid. Her pulse-rate was 140 per minute and her blood-pressure 105/60; rectal temperature 97·4° F. The abdomen showed slight distension with upper abdominal tenderness. Rectal examination revealed only a trace of apparently normal stool with no blood. In view of the child's deteriorating condition an intravenous infusion of plasma was begun, whilst blood was being cross-matched, and laparotomy was arranged.

OPERATION.—After induction of the anæsthetic a mass was palpable under the right costal margin and the abdomen was therefore explored through a right-sided transverse incision. Immediately the peritoneum was opened there came a great gush of blood—the whole peritoneal cavity was found to be awash with blood. When this had been partially cleared its source became apparent. On the under-surface of the right lobe of the liver was a large tumour which measured 2 in. × 2 in. × 1½ in. (*Fig.* 3). This had apparently fungated and broken down to produce the bleeding.

The only method of dealing with the situation appeared to involve the removal of the tumour together with surrounding liver tissue. This was done by applying an intestinal clamp loosely proximal to the line of section and then inserting a layer of overlapping mattress sutures behind this. No difficulty was experienced with hæmorrhage after this. Post-operative recovery was rapid despite a mild paralytic ileus. Formal right lobectomy was considered but in view of the pathology report it was held to be contra-indicated. Radiotherapy was undertaken but appeared to have no effect on the malignant process and the child died 2 months later.

AUTOPSY DETAILS (Dr. J. L. Emery).—The abdominal cavity contained approximately one pint of altered blood which appeared to have come from an ulcerated tumour of the liver. The liver itself was grossly enlarged by huge irregular masses affecting both lobes. On section there appeared to be multiple foci throughout the liver. There was no evidence of a primary source elsewhere.

The sections of the original tumour were examined by Professor R. A. Willis, who commented: "I feel sure that this is a primary hepatic tumour of the same class as that reported by Allison and myself (1956). The specimen shows predominance and great anaplasia of the epithelial element and relatively less osteogenesis. Its high degree of malignancy is shown also by the widespread invasion of the veins. This almost certainly means that intra-hepatic metastasis has taken place and the recurrence is therefore inevitable." This confirmed the view of Dr. Emery that this was a hepatic embryoma.

2. INTRAHEPATIC HÆMORRHAGE.—Rolleston and McNee (1929) write at some length on the question of bleeding and primary hepatic tumours. They state that extravasation into the necrotic growth may be sufficiently gross to produce faintness and collapse, and as a result of the bleeding a fluctuant tumour may be felt and mistaken for a liver abscess. Intermittent pain from recurrent bleeding may mislead the clinician as *Case* 2 demonstrates.

Case 2.—Gerald L., aged 8 months. This child was admitted to the City General Hospital, Sheffield, with a story of constipation which had been present for one week.

FIG. 4.—Invasion of the capsule by tumour—*Case* 2. (× 90.)

For the three days prior to admission there had been vomiting which was at times projectile. During the whole period there were intermittent attacks of pain during which the infant would pull its knees up to its abdomen and scream. In between the attacks he appeared to be pain-free. On the day of admission the bowels had been opened three times, the resulting motion being loose but containing no blood. On examination the child proved to be very irritable; the abdomen was not tense and a mass was palpable in the right hypochondrium. The rectum

was empty and the examining finger was not blood-stained on withdrawal.

A tentative diagnosis of recurrent intussusception was made and laparotomy was undertaken.

OPERATION.—The abdomen was explored through a right upper paramedian incision and a much enlarged liver was apparent—the right lobe being chiefly affected, in its lower half. The cause of the enlargement was obviously tumour, either primary or secondary, and a biopsy was taken before closing the abdomen.

The child died the day after operation following inhalation of vomitus.

PATHOLOGICAL DETAILS.—Autopsy was performed by Dr. J. L. Emery and the following is an extract from his report:

"The peritoneal cavity showed only a few cubic centimetres of clear fluid.

"*Liver*.—The lower half of the right lobe is grossly enlarged with nodular and cystic masses—small, white nodules being present on the surface.

"*Histology*.—The part of the liver separate from the tumour appears to be normal. The tumour consists of a mixed mass of tissue containing cartilage (*Fig.* 1), connective tissue, glandular epithelium, and masses of primitive cells. There are many hæmorrhages well into the tumour. It appears to be partially encapsulated in that there is a thin layer of connective tissue surrounding some parts of it. Other parts of the tumour do not appear to be encapsulated but appear to be invading (*Fig.* 4). The tumour in these areas is also mixed.

"*Comment*.—The tumour appears to be an embryoma of the liver analogous to the common embryoma of the kidney."

An intrahepatic hæmorrhage presumably frequently precedes bleeding into the peritoneal cavity. At times, however, the rupture may be anticipated and prevented by adhesion of greater omentum and transverse colon to the area.

3. SUBPHRENIC HÆMORRHAGE.—Bleeding may occur into a subphrenic space instead of into the general peritoneal cavity, as Lazarus and Friedmann (1953) have described. It is interesting to note that their patient, a woman of 67 years, had five years previously undergone resection of a massive liver tumour extending into the pelvis! Examination of the removed specimen revealed it to be a benign adenoma, yet at final autopsy the tumour then found was undoubtedly malignant with multiple foci throughout the liver. Her terminal illness was thought to be due to a subphrenic abscess as she was acutely dyspnœic, had signs of a basal pneumonia, and had a much elevated right diaphragm. At operation a massive subphrenic hæmatoma was found. Tumour was widely present in the liver and metastases studded the abdominal aspect of the diaphragm.

Subphrenic hæmatoma is a diagnosis which may be made more frequently than its occurrence merits, for, as several authors point out, the hepatic enlargement in primary liver tumour is often upwards rather than down into the subcostal regions of the abdominal cavity. This, together with some fixation to the dome of the diaphragm and local pain, may strongly suggest a subphrenic hæmatoma.

SYMPTOMATOLOGY

Abel (1934) quotes a series of 164 cases which were analysed by Eggel. The common symptoms in order of frequency were jaundice (61 per cent), ascites (58·5 per cent), œdema (41 per cent), and pyrexia (14 per cent). Hæmorrhage is not mentioned.

Rolleston and McNee (1929) stress that pain is common and may be the first symptom. There may be either a constant local pain or biliary colic if the mass should encroach upon the common bile-duct. They recognize hæmorrhage arising from both primary and secondary tumours of the liver.

In a series of 9 children with tumours of the liver, abdominal discomfort, a nagging local pain, and an abdominal mass were the rule (Ladd and Gross, 1941). Apparently no case presented as an abdominal catastrophe.

Cleland (1959) quotes indefinite symptoms such as irritability, restlessness, vomiting, as being the commonest symptoms amongst children. Local pain and an abdominal mass were the more specific but less common symptoms and it is these two which most commonly constitute the basis of a pre-operative or pre-autopsy diagnosis. The experience of finding an abdominal mass as the primary lead to a diagnosis is supported by the report of Packard and Palmer (1955) who found such a mass, often initially discovered by a parent, amongst all 6 of their malignant cases in children. *Case* 3 so presented.

Case 3.—Timothy W., aged 9 months. This infant was admitted because of general malaise associated with pyrexia and vomiting which had lasted for 5 days. Superficial examination revealed a distended abdomen and on questioning the mother remarked that this had been so since birth. Palpation of the abdomen immediately led to the finding of a massive, hard, irregular tumour filling the upper abdomen and extending below the umbilicus. This was thought to be the liver. The child was very pale and hæmoglobin estimation gave a figure of 8·3 g. per cent (56 per cent). Marrow puncture from three sites was performed to try to confirm or exclude a diagnosis of neuroblastoma and no typical neuroblastoma cellular elements could be identified. Examination of the urine showed neither infection nor blood, whilst liver function tests performed were within normal limits. Exploration of the tumour was then felt to be indicated and after correction of the anæmia this was undertaken.

OPERATION (Mr. R. B. Zachary).—The abdomen was opened through a transverse incision extending to the right costal margin at the level of the ninth rib. The right lobe of the liver was found to be enlarged to a very gross degree by tumour tissue (*Fig.* 5) and there was no obvious alternative primary source in the abdomen.

As the left lobe appeared to be normal an attempt at resection was thought justifiable. The incision was extended into the chest and the diaphragmatic connexions of the liver were divided. As a first step, control of the inferior vena cava above the diaphragm and below the liver by rubber tubing was obtained (*Fig.* 6). The possibility of successfully dividing the hepatic veins from the right lobe was then confirmed. Attention was next turned to the porta hepatis. The cystic duct was divided together with the branches to the right lobe of the portal vein and the hepatic artery after their course had been fully displayed. A line of demarcation then appeared on the liver showing clearly the boundary between the two functional lobes of the liver. The hepatic veins were divided and the right lobe was excised by diathermy. What oozing there was proved to be quite easily controlled by interlocking mattress sutures and at the end of the procedure the remaining left lobe was almost dry (*Fig.* 7). Closure of the wound with drainage to the chest and abdomen completed the operation.

The infant appeared well at the end of the operation and was returned to the ward with continuous intragastric suction to minimize the risk of inhalation of gastric contents. Unfortunately, despite this, he collapsed suddenly twelve hours later and died. The autopsy report

(Dr. Emery) read: "The operative procedure appears to have been completely adequate and I have been unable to find the naked-eye presence of any secondary or other deposits in the child." The cause of death was probably chiefly pulmonary collapse secondary to inhalation of regurgitated intestinal contents. The absence of secondary deposits was confirmed later by detailed microscopic examination of tissues from numerous sites. The resected

FIG. 5.—The right lobe of the liver (*Case* 3) grossly enlarged by tumour.

lesion proved to be a mixed hepatic tumour of the embryomatous pattern.

A more detailed account of the technique will be found in the writings of Pack, Miller, and Brasfield (1955). Whilst this formal procedure is a relatively recent innovation, it should be remembered that resection of liver for tumour is no novelty and Moynihan in 1914 could write that it was a legitimate surgical procedure with which every surgeon should make himself familiar.

DIFFERENTIAL DIAGNOSIS

The most likely diagnosis on finding a mass in the liver must be a secondary deposit from a primary tumour elsewhere. It was in the latter half of the nineteenth century that pathologists realized, through the teaching of Virchow, that tumours in the liver were almost always metastases, often from an occult primary source, and awareness of the true rarity of primary liver tumours grew (Abel, 1934). Prior to this, primary malignant disease was held to be common in the liver. In the adult the primary focus may be found in numerous sites, although most commonly in the alimentary tract. During infancy neuroblastoma and Wilms' tumours are the most likely source.

When intraperitoneal hæmorrhage occurs, the differential diagnosis lies between other causes of bleeding of similar dimensions. These include trauma to the liver or spleen, ruptured ectopic pregnancy, and volvulus or internal strangulation of a loop of bowel with an ensuing bloody transudate. Acute hæmorrhagic pancreatitis or mesenteric vascular catastrophes can also simulate the picture seen. Rupture of the tumour into a subphrenic space may strongly suggest a subphrenic abscess.

Intrahepatic hæmorrhage leads to localized pain and tenderness with possibly a palpable mass. This mass may be firm or fluctuant. Acute cholecystitis, empyema of the gall-bladder, acute pancreatitis, or localized perforation of a peptic ulcer may all be considered as possible diagnoses. Intermittent bleeding into the tumour in *Case* 2 produced attacks of screaming from the infant; this, with a mass in the hypochondrium, led to a pre-operative diagnosis of intussusception.

FIG. 6.—Control of the inferior vena cava above the diaphragm and below the liver prior to right hepatic lobectomy in *Case* 3.

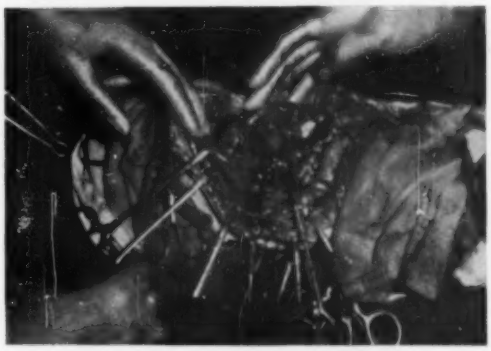

FIG. 7.—The remaining physiological left lobe after right hepatic lobectomy in *Case* 3.

INCIDENCE

In any Western community primary malignant liver tumours are rarely seen. Amongst the Bantu of Africa, the Javanese, and Japanese it is one of the commonest of cancers. Estimation of the incidence of the disease amongst occidentals is difficult, but Steiner (1938) assessed the occurrence in European and American hospitals as 144 from a series of 65,501 autopsies (0·219 per cent of autopsies). He accepted 75 cases from the literature in children under the age of 16 as genuine. Amongst these 75 there were 51 (68 per cent) boys and 24 (32 per cent) girls. Below the age of 3 there were 41 cases, 30 being boys. Cleland (1959) found only 10 hepatic malignant tumours in the records of the Children's Hospital of Los Angeles over a period of 57 years, whilst Packard and Palmer (1955) found 6 cases amongst 126,000 admissions over 14 years at Denver Children's Hospital.

PROGNOSIS

Primary cancer of the liver must be accepted at the moment as the master of all therapeutic manœuvres. So rare is any degree of success that writers record survivals of several months after surgery with awe. The 3 cases recorded here died —the tumour in 1 case appearing to blossom forth under the warmth of the radiotherapeutic beam! Surgical attack offers minimal hope of success but is justifiable if the diagnosis is not certain, as the lesion resected may prove to be benign.

SUMMARY

The clinical and pathological views on primary malignant disease of the liver are reviewed. The problem of its occurrence in infancy is discussed in more detail. The hopelessness of all forms of therapy at the moment is stressed. Three new cases are added to the literature—each illustrating a different point in the variable course of the disease. They are of interest chiefly because of the histological diagnosis of embryoma which appears to be a much rarer tumour than the carcinoma.

Acknowledgements.—I wish to acknowledge the assistance given to me in the preparation of this paper by Mr. R. B. Zachary who, together with Mr. J. T. Chesterman, allowed me to publish these cases. Dr. J. L. Emery and Professor R. A. Willis have been equally kind in allowing me to quote from their pathological reports.

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ANGIOMATOSIS OF LIVER CAUSING FATAL HÆMORRHAGE

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INTRODUCTION

THIS paper records the sudden death of a 9-year-old girl, due to hæmorrhage from a vascular malformation of the liver. The case is reported because of the extreme rarity of this condition.

CASE REPORT

R.I.—Reg. No. 185416. At about 5 p.m. on Jan. 23, 1960, a 9-year-old girl was brought to the Radcliffe Infirmary complaining of lower abdominal pain for the past 18 hours. The pain, which was severe to start with, had slightly diminished by that time, but had not shifted to the right iliac fossa. She had vomited and opened her bowels once during this time. She had no headache, sore throat, cough, or increased frequency of micturition. She had an attack of tonsillitis about 10 days before admission which had lasted for about a week but from which she had made a complete recovery.

On examination, her temperature was 99·2° F. and pulse 100 per minute. Her tongue was furred and there was slight fœtor oris. The chest and heart were normal. Abdominal palpation revealed no sign of peritonitis. She was tender over the lower abdomen but less so over McBurney's point. The liver and spleen were not felt and rectal examination revealed nothing. Urine was normal.

No firm diagnosis was made and she was admitted for observation. Five hours after admission she no longer complained of pain and even the abdominal tenderness disappeared. Oral fluids were then allowed.

On the following day she was symptom-free and no abnormality was found on examination. A light diet was given and she spent the day playing in the ward. At 5.15 a.m. on Jan. 25 she collapsed suddenly after getting up to pass water. When seen immediately afterwards she was pale and unconscious, her blood-pressure being unrecordable and her pulse barely perceptible. Abdominal palpation revealed no guarding or mass, and no bowel sounds were heard. Rectal examination was normal and no blood was seen on the glove. A diagnosis of circulatory failure was made, due probably to internal hæmorrhage.

A saline drip was started, and this proving ineffective, unmatched group O Rh-negative blood was given. She showed no improvement and died at 6.40 a.m.

POST-MORTEM FINDINGS (R.I., P.M. No. 84/60).—The body was that of a moderately built young girl. There was nothing significant on external examination.

On opening the abdomen about 800 ml. of free blood was found in the peritoneal cavity. The liver which weighed 1420 g. had numerous bluish spidery marks on its upper sub-capsular surface. The inferior surface showed marked bluish mottling. There was a tear in the

capsule of the liver near the anterior edge of the left lobe and it was here that a sub-capsular hæmorrhage had burst into the peritoneal cavity (*Fig.* 8). A considerable quantity of clotted blood was still present in the sub-capsular space of the liver. The cut surface of the liver showed that it was riddled with huge spaces filled with clotted blood (*Fig.* 9). These big spaces appeared to be cavernous sinusoids (conveniently called cavernoids) and their size varied from pinhead to about 5 mm. in diameter. The whole of the liver substance was uniformly involved and the liver tissue between these cavernoids was rather soft and granular.

Apart from mild catarrhal changes in the respiratory passages there was no significant finding in other organs.

Pieces of liver were fixed in 10 per cent formal saline, embedded in paraffin and stained by (1) Hæmatoxylin

FIG. 8.—The inferior surface of the left lobe of the liver showing the rupture in the capsule and mottled surface.

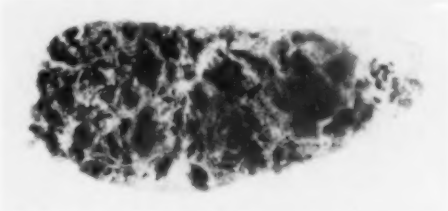

FIG. 9.—The cut surface of the liver showing giant sinusoids filled with clotted blood.

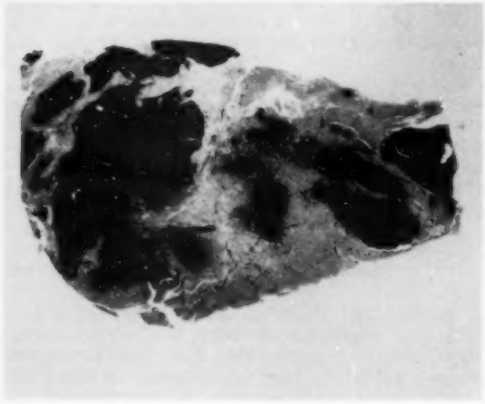

FIG. 10.—A close view of the cavernoids (giant sinusoids).

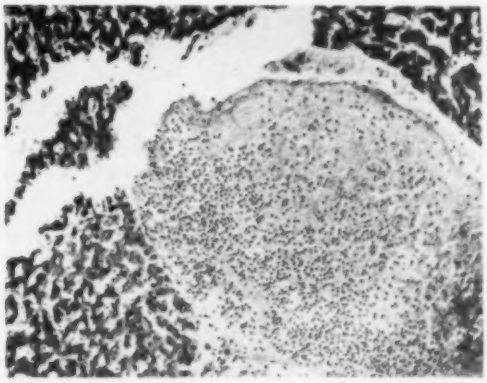

FIG. 11.—A low-power view of a cavernoid showing the separation of white and red cells. On the upper right the sinusoidal endothelium is seen to be displaced inwards, creating a space between it and the hepatic parenchyma. The space on the upper left is an artefact. H. and E. (× 40.)

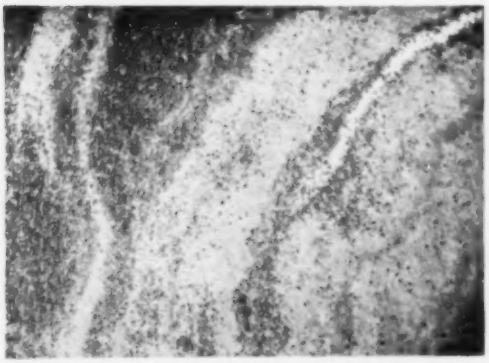

FIG. 12.—A low-power view of an ante-mortem thrombus in a cavernoid showing the lines of Zahn. H. and E. (× 40.)

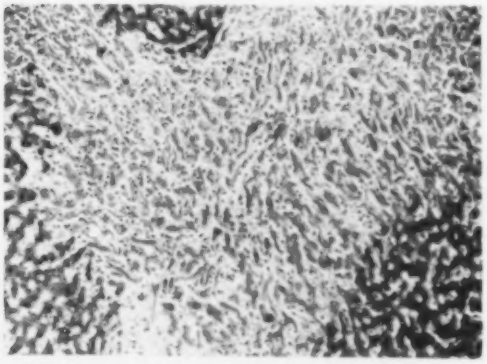

FIG. 13.—A localized hæmorrhagic area of necrosis in hepatic parenchyma. H. and E. (× 40.)

and eosin, (2) van Gieson, (3) Phosphotungstic acid hæmatoxylin, (4) Robb-Smith's method for reticulin, and (5) Perl's Prussian blue for iron.

The sections showed numerous spaces filled with blood (*Fig.* 10). Most of these were lined by endothelium, but some were simply lined by hepatic cells (*Fig.* 11). The endothelial lining, however, was displaced inwards at certain places creating a space between it and the hepatic parenchyma. This space was usually filled with fibrin. No Kupffer cells could be made out in the walls of the cavernoids. In some of these cavernoids the red cells had settled out and were separated from the plasma. In others the leucocytes had a tendency to aggregate towards one side of the cavernoids (*Fig.* 11). At places blood had burst through the endothelium and entered the parenchyma, causing some disruption of the cells. At least one cavernoid contained an antemortem thrombus with lines of Zahn (*Fig.* 12). The liver cells between the cavernoids showed patchy areas of necrosis and some of these areas were either infiltrated with some polymorphonuclears or were distinctly hæmorrhagic (*Fig.* 13). These areas had no definite relation to either the portal tracts or central veins. The portal areas showed slight increase in connective tissues. The central veins were normal. There was no condensation of reticulin and no iron was deposited either in the liver cells or in the Kupffer cells of normal sinusoids.

A diagnosis of 'diffuse angiomatosis of liver' was made. The initial pain in the abdomen was due, perhaps, to the sub-capsular hæmorrhage and the final collapse was due to the rupture of the liver capsule causing hæmoperitoneum.

DISCUSSION

Angiomatosis of the liver is a developmental malformation of the blood-vessels, in which the liver substance is traversed by giant sinusoids lined by vascular endothelium but devoid of Kupffer cells. Diffuse angiomatosis involving the whole of the liver is an extremely rare condition. Willis (1953) in his book has given a photomicrograph of this condition in a newborn infant, though the appearance of the liver in his case is very different from ours. Localized forms of this condition, however, are not uncommon, most of the so-called 'hæmangiomas of the liver' being examples of this condition. They are therefore not true tumours but are hamartomas. Jaffé has reviewed the literature of these 'tumours' up to 1929.

The diagnosis of diffuse angiomatosis of the liver would be extremely difficult during life and this is because it does not produce many clinical manifestations. Hæmorrhage was the only complication in our case and proved fatal. The liver in this case was not palpable during life and at autopsy its weight was within normal limits. However, as hæmangiomas of the liver can produce localized swellings, it is possible that in certain cases diffuse angiomatosis may also cause hepatomegaly. In the absence of any injection studies we cannot be certain about the exact circulation in the cavernoids, though most probably they were fed by the portal vein. A portal venogram during life may show interesting appearances in this condition. From our material we have no reason to believe that diffuse angiomatosis can cause hepatic dysfunction as sufficient liver tissue has been spared. In Willis's photomicrograph, however, there is hardly any normal liver tissue to be seen and a condition of that severity would certainly be incompatible with life.

At autopsy diagnosis is quite easy. Big cavernoids involving the whole of the liver, lined by vascular endothelium and without any evidence of malignancy, are diagnostic of this condition. The only condition which may have to be excluded is a rather ill-defined entity called 'peliosis hepatis'. Senf (1939) discussed this condition at length and Zak (1950) collected about 30 cases from the literature, adding 1 of his own. In this condition localized areas of necrosis appear in the liver followed by hæmorrhage into them and the formation of blood-cysts. It follows prolonged congestion of the liver, usually due to persistent coughing, and is commonly associated with pulmonary tuberculosis. In peliosis hepatis blood-cysts are small (the largest in the case of Young (1953) were 2 mm. in diameter), and are usually without an endothelial lining, although some with an endothelial lining have been described. Though areas of necrosis, which are an essential prerequisite to the development of peliosis hepatis, were present in our case, they were most probably due to the hæmodynamic disturbances in the liver following the sub-capsular hæmorrhage. The rupture of the delicate endothelial lining of the cavernoids, again probably due to sub-capsular hæmorrhage, can explain the presence of blood in these necrotic areas as in certain areas of the normal liver tissue.

SUMMARY

A case of diffuse angiomatosis of the liver is described in a young girl who died suddenly after a short history of abdominal pain. The pathological findings in the liver are described with special reference to peliosis hepatis.

Acknowledgements.—We are very grateful to Dr. A. H. T. Robb-Smith and Mr. Elliot-Smith for their permission to publish this paper.

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HEPATIC LOBECTOMY IN INFANCY FOR HEPATOBLASTOMA

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PRIMARY liver tumours in children are extremely uncommon (Edmondson, 1956). Packard and Palmer (1955) report an incidence of 9 cases in 126,000 admissions to a children's hospital. They also note that the majority of liver tumours in children are malignant. Gross (1953), too, out of 18 cases of hepatic tumour found 13 to be malignant.

Most of these tumours have been reported as hepatomata or as hepatic mixed tumours. In 1948 Willis defined the hepatoblastoma as an embryonic tumour of the liver, analogous to Wilms' tumour of the kidney. He emphasized that the distinction between hepatoma and hepatoblastoma is a very fine one and at times almost impossible to make. Bodian and White (1952) found 8 hepatoblastomata in a series of 10 primary malignant liver tumours in infants; Debre, Mozziconacci, Habib, and Habib (1954) reported 1 case and reviewed 27 others which they considered could be classified as hepatoblastomata; Florentin, Rauber, and Macinot (1956) reported an infant who died 35 min. after birth and in whom a large hepatoblastoma was found.

Most liver tumours in children occur below the age of 2 years. Steiner (1938), in a review of 77 cases of primary liver cancer in children, found 41 which developed before the age of 2 years; Millman and Grayzel (1951) found that one-third of their series of 27 cases of mixed liver tumours were under 1 year old; in Bigelow and Wright's (1953) series of 95 cases, 55 were under 2 years old. Although the sex incidence differs in various series, it appears that malignant liver tumours are more common in male children.

A hepatoblastoma in an infant aged 7 months is reported. The tumour was excised and after 4 years there has been no recurrence. It appears to be the first long-term survival of hepatoblastoma in the literature.

CASE REPORT†

A female infant, P. C., aged 7 months, was admitted to the pædiatric unit of the Woolwich Memorial Hospital, the mother having noticed a lump in the child's abdomen on the previous day. The child, a first-born, weighed 7 lb. 5 oz. at birth, and had been under out-patient treatment at another hospital for a congenital contracture of the fingers of the left hand. She had always been difficult to feed, but had added 4 lb. 6 oz. to her birth weight.

CONDITION ON ADMISSION.—Though small for her age, she was a well-nourished, active, alert, and happy child. The left arm was noticeably smaller than the right, and there was a flexion deformity of the left hand. There was a benign pigmented mole on the dorsum of the left foot.

Inspection of the abdomen revealed a mass below the left costal margin (*Fig.* 14). Palpation showed it to be a firm globular tumour. It was thought to be either an enlarged left lobe of the liver or a tumour lying in the liver. The spleen and kidneys were not enlarged, nor were any other masses palpable in the abdomen. Rectal examination revealed no abnormality.

INVESTIGATIONS.—Chest radiograph was normal. Straight radiography of the abdomen showed a large mass in the upper abdomen which displaced the small bowel downwards and to the right. Blood-count: Hb 13·9 g. per cent; W.B.C. 9000/c.mm. The differential count was normal, as were the red cells and platelets. W.R. was negative and liver function tests were normal. There were no abnormal constituents in the urine. Examination of the stools revealed no abnormality and normal tryptic activity.

FIG. 14.—Lateral view of abdomen. Tumour clearly visible below left costal margin.

PROGRESS.—The child was difficult to feed, apparently having no interest in food. However, in the first few days in hospital, while under investigation, she gained 9 oz., but the tumour appeared to be increasing in size and it was decided to explore the abdomen without further delay.

LAPAROTOMY (Sept. 20, 1956) (Mr. H. E. Lockhart-Mummery).—With the back hyperextended, a long transverse incision in the upper abdomen exposed a globular tumour, the size of a tennis ball, occupying nearly the whole of the left lobe of the liver. The right lobe and the rest of the abdominal contents were normal. It was therefore decided to perform a left hepatic lobectomy.

The left lobe of the liver was mobilized and it was apparent that the tumour did not invade the right lobe, the vena cava, or the porta hepatis. The left hepatic vein was divided between ligatures, as were the left branch of the portal vein, the left hepatic artery, and the left hepatic duct. A bulldog clamp was now applied to the structures in the hepatoduodenal ligament, and the left lobe of the liver was then excised by cutting through normal liver tissue along the line of attachment of the falciform ligament. The large sinuses of the raw liver surface were underrun with catgut sutures. The bulldog clamp was then removed, having been kept on for 15 min., and complete hæmostasis was secured. The raw surface of the liver was closed by approximating the

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† This case was shown at a meeting of the Section of Pædiatrics of the Royal Society of Medicine on Nov. 28, 1958.

anterior and posterior capsules. The wound was closed with drainage.

POST-OPERATIVE COURSE.—A blood transfusion had been commenced during the operation and was continued in the ward. Soon after her return there was a sudden deterioration in the infant's condition; the pulse became very rapid and feeble and the blood-pressure unrecordable. About 150 c.c. of blood were rapidly transfused under pressure and she improved. Seven hours post-operatively she developed a transient hæmoglobinuria. The transfused blood was re-checked, but no incompatibility could be demonstrated and no antibodies were found in the child's serum. Eighteen hours after operation she developed a rapidly increasing jaundice. The serum-bilirubin rose to 6·3 mg. per cent. The jaundice subsequently cleared fairly rapidly and by the fourth day was no longer apparent. On the second day after operation she developed a pyrexia, which continued for 12 days, despite penicillin and terramycin therapy. This was accompanied by a polymorphonuclear leucocytosis, but there was no clinical evidence of any infection.

FIG. 15.—Specimen removed at operation. Entire left lobe of liver.

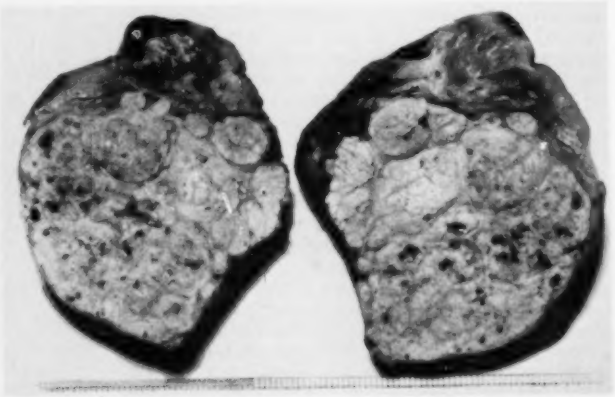

FIG. 16.—Cut section of left lobe of liver. The tumour almost completely occupies the whole of the lobe.

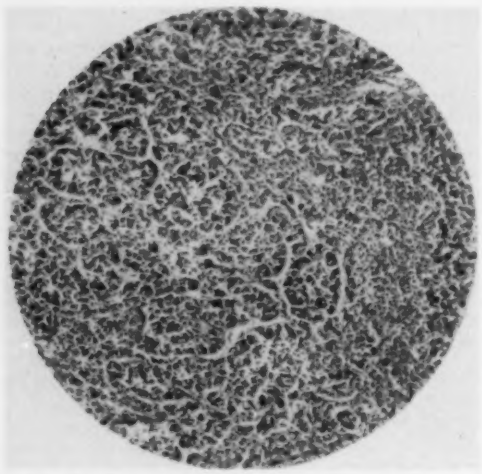

FIG. 17.—Low-power view of section of tumour. H. and E. (× 66·5.)

PATHOLOGICAL REPORTS.—

Dr. J. D. W. Williams: Specimen consists of the left lobe of the liver and contains a solid tumour 7·5 cm. × 6·5 cm., and 5 cm. thick (*Fig.* 15). On cut section there is a fringe of normal liver with a uniform homogenous greyish-white tumour which has the macroscopical appearance of encapsulation (*Fig.* 16). At one pole there are hæmorrhagic areas.

Dr. M. Bodian: The section shows massive neoplastic change of two cell types: some simulating liver cells, though without any lobular architectural arrangement, others simulating primitive bile-duct epithelium. There are numerous mitotic figures and in some areas pseudo-rosettes (*Fig.* 17).

The appearances are those of a highly malignant hepatoblastoma.

Professor R. A. Willis: Typical example of an embryonic hepatoma comprised wholly of immature liver cells. Although it appeared well circumscribed and is fairly well-differentiated, the number of mitoses and invasion of the small veins at the margin in places show it is a malignant growth and metastasis to the lungs is a considerable risk.

FOLLOW-UP —Since operation, the child has received vitamin B_{12}, 1000 μg. twice weekly. This was given because of the similarity between hepatoblastoma and neuroblastoma, the latter having been found to respond to large doses of vitamin B_{12} (Cade, 1957).

She has been followed up regularly and remains well 4 years after operation, with no evidence of metastases. She is now a normally developed child for her age.

DISCUSSION

The techniques of excision of liver tumours and of partial hepatectomy are by no means new to the surgeon's armamentarium. The first planned partial hepatectomy was performed in 1888 by Langenbuch and in 1899 a review of 76 cases of local excision was published by Keen, who was the first to remove the entire left lobe of the liver. In 1954 Brunschwig reported on more than 500 patients of all ages from whom liver tumours had been removed, and in 1955 he published his personal experience of 12 right and 10 left hepatic lobectomies. The vast majority of the above operations were done on adults. In children there are very few reports indeed of successes

following resective surgery for liver malignancy (*Table I*).

The survivals reported above illustrate the value of early excision for malignant liver tumours in children. Without treatment the average duration of life is 4–6 months from the onset of symptoms (Debre and others, 1954; Bodian and White, 1952; Bigelow and Wright, 1953). Apart from the possibility of displaying a benign tumour or cyst, a precise assessment of the operability of a malignant tumour can only be made at laparotomy. Major resective surgery, despite its relatively high mortality, offers the only chance of successful treatment. Bodian (1957) found the results of radiotherapy to be very poor. Phillips and Murikami (1960) report on 5 children who survived 8 months after irradiation and an average of 13 months after the appearance of the first symptom.

Table I.—Successful Partial Hepatectomy in Children for Primary Liver Malignancy

Author	Pathology	Age of Patient at Time of Operation	Length of Survival
Yarbrough (1944)	Teratoma	7 wk.	3 yr.
Donovan and Santulli (1946)	Mesenchymoma	6½ yr.	6 yr.
Lorimer (1955)	Mesenchymoma	15 yr.	8 mth.
Tweedy (1956)	Hepatoblastoma	?	10 yr.
Brunschwig (1957)	Hepatoma	14 yr.	5 yr.
Knox, Zintel, and Begg (1958)	Hepatoma	12 mth.	2½ yr.
Cleland, (1957)	Carcinoma	10 yr.	8 mth.
Borman, Harbott, and Morris, (1961)	Hepatoblastoma	7 mth.	4 yr.

It is not the purpose of this paper to discuss the technique of hepatic lobectomy. However, an interesting feature of the technique employed in our patient was the clamping of the structures in the hepatoduodenal ligament. This had previously been reported by Clatworthy and Boles (1956), who did a left lobectomy in a child for benign lymphangioma and clamped these structures for 6 min. without ill effects. In our child these structures were clamped for 15 min., and, although hæmorrhage was reduced during the actual liver resection, the clamping may well have been responsible for the post-operative fever and jaundice. On the other hand, the administration of blood under pressure through a small cannula when the child was in shock may have led to hæmolysis, jaundice, and hæmoglobinuria.

Hepatoblastoma is an extremely malignant tumour. Bodian (1957) has not had a survivor in all 13 cases in his experience. One case lived 3 years after exploratory laparotomy (Debre and others, 1954); another survived 10 years following excision (Tweedy, 1956). Our patient has lived 4 years since the operation and the prognosis appears to be good. She has survived the Collins 'period of risk' and although the latter work was done on Wilms' tumour (Collins, 1955), it applies to all embryonic neoplasms (Collins, 1960).

SUMMARY

Successful left hepatic lobectomy for hepatoblastoma in an infant aged 7 months is described. The child has survived 4 years and is free of metastases.

An account of the operative technique and post-operative course is given.

A review is presented of children surviving after excision of malignant liver tumours.

The prognosis and treatment of primary liver malignancy in infants are discussed. Early radical treatment is strongly recommended.

Acknowledgements.—We wish to thank Mr. H. E. Lockhart-Mummery for his advice in the preparation of the paper and the department of photography of the Woolwich Memorial Hospital for the photographs.

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MALIGNANT HEPATOMA IN A BOY AGED 7 YEARS

WITH POST-OPERATIVE SURVIVAL FOR OVER 3 YEARS

By P. K. A. McWILLIAM*

PONTEFRACT GENERAL INFIRMARY

APPROXIMATELY 100 cases of malignant hepatoma in children have been reported, the majority occurring in children under the age of 3 years. Almost invariably the condition was rapidly fatal, and in the few cases where resection was attempted many children died in the immediate post-operative period or shortly afterwards.

The following patient is considered worthy of record because of his age, the long duration of symptoms before operation, and the relatively long period of post-operative survival with reasonable comfort.

CASE REPORT

A farmer's son, aged 7 years, was admitted to hospital on Nov. 23, 1955, with a year's history of intermittent vomiting and a gradually enlarging abdomen, which the parents ascribed to a blow following a fall. He was otherwise in apparently good health and medical aid was sought in the middle of November, 1955, because of a week's history of lassitude, nausea, and diarrhœa. Both parents were young and well, the boy's sister was well, and there was no relevant family history.

FIG. 18.—Excised left lobe of liver showing the hepatoma.

ON EXAMINATION.—Physically he was a well-nourished boy of good colour, who did not appear ill. There was a large abdominal mass extending to five fingerbreadths below the right costal margin and extending diagonally up to and under the left costal margin. The lower edge of the mass was sharp and its consistency was uniformly hard. Rectal examination was negative and no other abnormal physical signs were detected.

Investigations.—

Blood: Hæmoglobin 90 per cent (Haldane); Total white cells 8500/cu.mm.

Differential White-blood Cell-count: Polymorphs 55 per cent; Eosinophils 7 per cent; Lymphocytes 37 per cent; Monocytes 1 per cent.

Blood-film: The red cells appear normal; platelets are numerous.

B.S.R.: 22 mm. in 1 hr. (micro method).

Liver Function Tests: Plasma Van den Bergh; Direct reaction. Very faint pink colorization after 45 min. Plasma-bilirubin, within normal limits. Serum thymol turbidity, 2 units. Serum alkaline phosphatase, 14 King-Armstrong units.

Urinalysis: Albumin + Sugar—nil, no deposit. Bile-salt (Hay's test), negative. Bile-pigment (Fouchet's test), very weak positive. Urobilin (Schlesinger's test), trace.

Mantoux Reaction: ($\frac{1}{1000}$): Negative.

Radiology: Chest shows normal appearance. The abdomen shows considerable soft-tissue shadowing, spreading from the right hypochondrium, consistent with liver enlargement. An intravenous pyelogram was normal.

A Casoni skin-test for hydatid disease was done, especially in view of the high eosinophil count and the fact that the patient lived on a farm. This was negative.

AT OPERATION.—Exploratory laparotomy was decided upon and this was carried out by Mr. J. A. Rhind on Dec. 6, 1955. A very vascular tumour was found projecting from the under surface of the left lobe of the liver and extending almost to the hilum. The tumour extended across the midline in the region of the inferior vena cava, thus making complete resection of the neoplasm impossible. The left lobe of the liver was excised (*Fig.* 18), but a piece of tumour tissue, the size of a golf ball, remained attached to the inferior vena cava.

There was considerable blood-loss, which was replaced by immediate transfusion, and the raw surface of the liver continued to bleed profusely until the hæmorrhage was eventually arrested by diathermy and packs. The post-operative course was surprisingly uneventful. No further bleeding occurred and a sinogram, after removal of the pack, revealed that the wound was healing well. The patient was discharged home on Christmas Eve, 1955, and recommenced school six weeks afterwards.

PATHOLOGY.—Professor R. A. Willis very kindly reported on the tumour sections as follows: "This is a typical specimen of malignant hepatoma (liver-cell carcinoma), a well-known tumour of infancy and childhood. These growths frequently metastasize in the liver itself and to the lungs and an X-ray examination of your patient's chest would be wise. The tumours often secrete bile and stain themselves green, even in their metastases."

FOLLOW-UP.—Three months after operation some hardness was felt in the epigastrium, and six months after this tumour masses were palpable behind the scar and a hard liver edge was palpable 1 in. below the costal margin. Apart from a little pallor, the patient looked well and, although not attending school, he was playing out of doors on most days. He had occasional bouts of vomiting. A chest radiograph on Sept. 26, 1956, just over nine months after operation, revealed numerous rounded secondary deposits (*Fig.* 19) which subsequently increased still further (*Fig.* 20) although physical signs in the chest were surprisingly few until the last few months of his life.

In March, 1957, fifteen months after operation, the patient was playing and walking comfortably despite numerous, hard, round tumour masses which were readily palpable through the abdominal wall, especially in the right hypochondrium and the suprapubic region.

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His abdomen became progressively more distended, first with secondary deposits of increasing size and number and, later, with free fluid. At the end of 1957 he began to have peripheral œdema and dyspnœa.

By this time frequent transfusions of packed red blood-cells were being given to counteract his anæmia. Also, large doses of vitamin B_{12} (1000/μg. twice weekly) were given to help correct a dietary deficiency of this vitamin, which was thought to be responsible for episodes of stomatitis.

In February, 1958, the patient had a severe attack of influenza and, although extremely ill, he recovered and

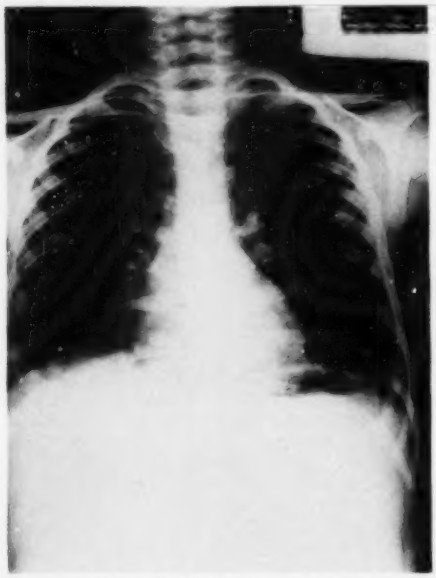

FIG. 19.—Radiograph of the patient's chest, nine months after operation, demonstrating secondary deposits.

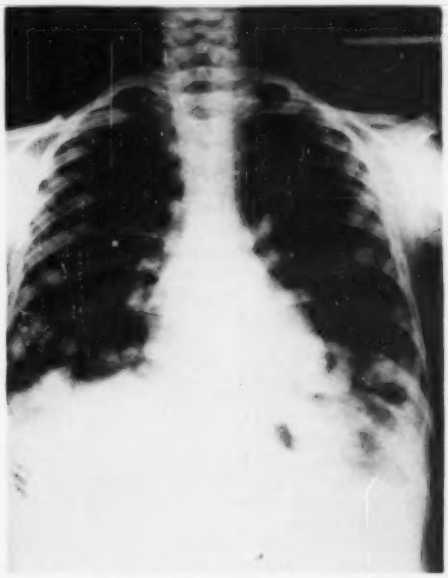

FIG. 20.—Radiograph of the patient's chest, twenty-one months after operation, demonstrating secondary deposits.

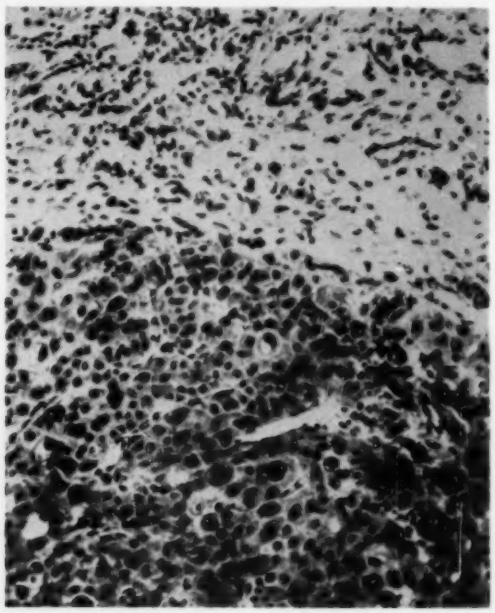

FIG. 21.—Photomicrograph showing boundary of tumour.

was surprisingly lively and active for the following three months. His hæmoglobin increased to between 65 per cent and 75 per cent (Haldane), and although his abdomen continued to increase in size, he was free from pain and was able to walk about slowly and play alone contentedly.

From June, 1958, onwards, he became progressively thinner and more emaciated. His peripheral œdema increased and this responded partially to chlorothiazide, 500 mg. daily, indicating that some degree of cardiac failure was causing the œdema as well as the venous obstruction; the transfusions ran with difficulty. His general condition deteriorated still further and he died at home in February, 1959. Post-mortem examination was not carried out.

Soon after the operation, radiotherapy was considered but was thought inadvisable, since histologically the tumour did not appear to be radio sensitive (*Fig. 21*). The possibility of giving antimitotic drugs to try to halt the growth of the metastases was also considered, but this was not done owing to the toxicity of these preparations (e.g., the nitrogen mustards and urethane) and their lack of specific effect on the liver.

DISCUSSION

Perusal of the literature reveals that primary malignant hepatomata in children occur usually within the first two years of life and in livers which are developmentally normal. Thus they are not superimposed on pre-existing cirrhotic lesions as in adults (Steiner, 1938; Edmondson, 1956; Clatworthy, Boles, and Newton, 1960).

Rarely, however, exceptions do occur, for Wentz and Kato (1940) described a primary carcinoma of the

liver in a boy of 6 years which was associated with Banti's syndrome. The changes included splenomegaly, cirrhotic liver changes, and œsophageal and gastric varices from which hæmatemeses occurred. The symptoms and signs of malignant hepatoma consist of an abdominal mass, anorexia, fever, loss of weight, pain, and rarely jaundice. Steiner considered that the average duration of symptoms, the onset of which could be sudden or insidious, was four months.

Clatworthy and others (1960) classified primary liver tumours in children into three groups, viz.: tumours of hepatic cell origin, i.e., hepatomata; tumours of supporting tissue, e.g., mesenchymomata; and mixed tumours, e.g., teratomata. They drew attention to the poor prognosis associated with hepatomata and stated that in their series of 15 patients with primary malignant liver tumours, none of the 10 patients with true hepatomata survived for more than six months after operation. Nevertheless, they consider lobectomy to be indicated in cases where there are no metastases and they describe the surgical technique for this.

Other workers have reported similar results. Some of the earlier cases died, either during the operation or in the immediate post-operative period (Steiner, 1938; Sawyer, 1950). O'Sullivan (1951) removed the left lobe of the liver of a girl aged 5 years suffering from hepatoma, but her condition deteriorated from the third post-operative month and, despite radiotherapy, she died just short of a year after operation.

So far, the longest recorded period of survival of a patient with a hepatoma would appear to be that of Lee, Newstedt, and Siddall (1956), who reported the spontaneous regression of a hepatoma (confirmed by biopsy) with the child in good health 10 years after the establishment of the diagnosis.

Several long periods of survival following operation or radiotherapy have been reported in respect of malignant liver tumours in children other than hepatomata. Anderson (1951) reported 1 long-term survivor in 12 cases over a 15-year period. Following excision of the left lobe of the liver for a mesenchymoma, the child survived for 6 years, whilst Gross (1953) reported 2 "cures". One was a 7-year survival following radiotherapy for multiple hæmangiomata of the liver, and the other was a survival period of 10 years after a wedge resection of liver for a hæmartoma.

The patient described in this article would appear unique in surviving for over 3 years after lobectomy for a true progressive malignant hepatoma, and his progress would support the view of Clatworthy and others that lobectomy for malignant hepatoma, in the absence of metastases, is a worthwhile procedure.

SUMMARY

The clinical history, diagnosis, and operative details of a malignant hepatoma in a boy of 7 years are described.

The post-operative survival, lasting over 3 years, is recounted.

A brief survey of the current literature is given, which indicates the poor prognosis of malignant hepatomata in children.

The view of other workers, that operation for hepatoma in the absence of metastases should be undertaken, is supported.

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I am also indebted to Dr. A. M. Fraser for the photographs and the radiological reports, and to Dr. E. L. Simons for the pathological investigations and the photomicrograph

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FLOW STUDIES ON THE HUMAN COMMON DUCT

WITH SPECIAL REFERENCE TO THE EFFECT OF SPHINCTEROTOMY

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THIS is the report of an attempt to compare the emptying properties of the common duct in patients in whom sphincterotomy had been performed with those in whom the sphincter had been left intact and to demonstrate differences in hydrodynamic properties between the two groups.

In 10 patients the common duct had been explored but the sphincter had not been sectioned. In a second group of 6 patients transduodenal sphincterotomy had been carried out. The problem was to decide whether sphincterotomy had any effect.

A B

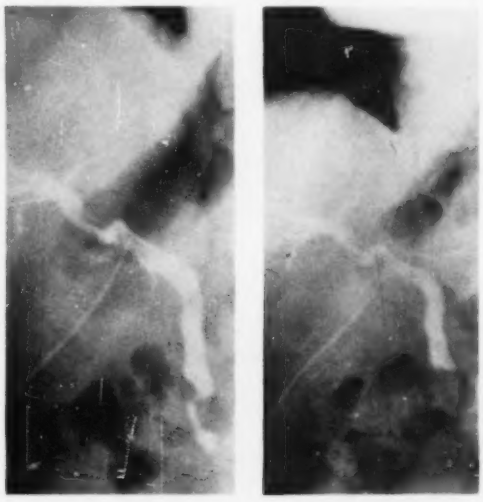
FIG. 22.—Two cholangiograms from a 49-year-old woman 10 days after exploration of the common duct. A, Shows free flow into the duodenum with slight pancreatic reflux. B, Shows the closure of the lower end of the duct by duodenal muscular spasm. This was taken 5 min. after 10 mg. morphine had been given intravenously. Note increase of pancreatic reflux.

All of the patients had undergone cholecystectomy and consequently no information on gall-bladder behaviour was obtained. From the experimental point of view, the fact that a cholecystectomy had been performed might be an advantage as any modifying influences due to the presence of the gall-bladder were eliminated.

CHOICE OF METHODS OF INVESTIGATION

The standard methods of investigation of environmental pressure and emptying behaviour of the biliary tree are cholangiography, pressure readings, and, more recently, study of pressure/flow relationships.

Post-exploratory cholangiography with the aid of radio-opaque solutions such as diodone and hypaque is too well known to require further explanation. It was initially thought that radiological studies might give an answer to the problem of whether sphincterotomy made a difference to flow in the common duct. Unfortunately, these hopes were not fulfilled. When diodone was run into the common duct via a T-tube, cholangiograms failed to show any difference in radiological appearances in the two groups. Therefore an attempt was made to stimulate the sphincter by means of drugs. Potent spasmogenic substances, such as pethidine and morphine, were used to provoke contraction of the sphincter. Unfortunately, not only the sphincter but the whole duodenal wall appeared to contract and there was no cholangiographic difference between those patients in whom sphincterotomy had been carried out and the others. The stimulus was obviously too crude to differentiate the actions of the choledochoduodenal muscle complex. The whole wall was thrown into spasm by morphine and this spasm was relaxed *in toto* by amyl nitrate. Cholangiograms taken before and after intravenous morphine in one patient out of each group are shown in *Figs.* 22, 23.



A B

FIG. 23.—Cholangiograms from a 60-year-old man 10 days after transduodenal sphincterotomy. A, Shows free flow. B, Shows effect of 10 mg. morphine given intravenously 5 min. previously. There is obliteration of the lower end of the duct.

Pressure studies have been carried out with varying success by many observers both in human and in animal subjects (Parry, Hallenbeck, and Grindley,

1955; Newman and Northup, 1957; Eisman, Brown, Virabutr, and Gottesfeld, 1959). Unfortunately, the pressure responses to stimuli such as gastric emptying and the injection of fluids down the T-tube were similar in the two groups of patients in the present series. Pressure recordings were unsatisfactory as an indication of flow. So gross are the changes in biliary pressure brought about by respiration, laughter,

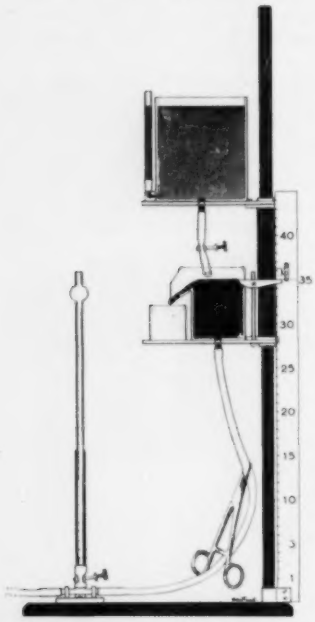


FIG. 24.—The apparatus devised for flow and pressure measurements. For description, *see* text.

straining, and postural change that they overshadowed the small changes noted in the duct when pressure was recorded continuously.

Since the task of the common duct is to allow the passage of fluid through its lumen, it was thought advisable to devise a simple experiment which would allow flow rates to be measured under various circumstances.

APPARATUS

An apparatus was designed (*Fig.* 24) to introduce measurable quantities of fluid into the common duct at predetermined pressures. A simple glass manometer of the Greenfield type was incorporated for pressure measurement and an upright rod carried two reservoirs. The lower of these was connected by rubber tubing to an adaptor and thence to the T-tube. This reservoir had a spillway at a level marked by a pointer. The effective level of the fluid above the base of the apparatus could be decided and varied at will by setting the pointer to any desired mark on a vertical metre scale. Excess fluid shed by the spillway was collected in a small plastic container. The upper reservoir was used to allow easy maintenance of the fluid level in the lower one. A side tube with an etched mark led into the upper container so that at the end of a period of flow the amount lost from the machine could be found by 'topping up' the upper reservoir to the mark. Thus, at various pressures and for various times, fluid could be introduced into the common duct by way of the T-tube and the volume perfused could easily be determined. When flow rates were small it was easier to use only the lower reservoir, keeping the level of fluid up to that of the spillway during flow by pouring directly from a measuring cylinder. All fluid lost from the apparatus in these experiments that had not gone over the spillway must therefore have gone into the patient.

EXPERIMENTAL CONDITIONS

There are many variables that may operate in a series of experiments such as were carried out, and as many as possible of these were investigated. The recordings eventually accepted were made under standard conditions.

Because there is often œdema at the choledochoduodenal junction after operation, recordings during the first ten days were excluded from the analysis. The majority of observations were made between the eleventh and sixteenth post-operative days.

A standard-sized T-tube was used. The best from the point of view of reasonable size and low resistance was found to be the Maingot No. 7 latex tube which has an internal diameter of 3 mm. Half of the circumference of the transverse limb of the tube was removed, the remaining part acting only as a retaining flange. The T-tube was secured in the duct as safely as possible at operation by closing the excess length of the choledochotomy incision by a continuous fine chromic catgut suture carried on an atraumatic needle.

The tube was brought out through a stab incision in the flank at the same distance from the back as the point of introduction to the duct. Kinking was carefully avoided within the abdomen and special care was taken to prevent constriction of the lumen of the tube by the cutaneous mooring suture.

At the tenth day the patient was screened and cholangiograms were taken. Particular care was taken to ensure that there was no leakage at the site of entry of the tube to the common duct. Any patients with such leaks were excluded from further study.

The base plate of the apparatus was set opposite the exit wound for the T-tube and all recordings were carried out with the subject lying supine with two pillows. To avoid the risk of duodenal pressure variation after gastric emptying, fasting subjects were used. The majority of observations were made between 8 a.m. and 9 a.m., the patient being allowed a cup of tea at 6.30 a.m., but no solid food.

Sterile normal saline was perfused at 37° C. It may be noted that the use of other fluids (e.g., 5 per cent dextrose), increase or decrease in temperature, and the administration of meals made no significant difference to the results.

The range of pressures used varied from subject to subject. The resting biliary pressure during quiet respiration is 9–11 cm. of water and flows at pressures from 10 to 45 cm. H_2O were studied. The normal range of pressures covering sitting, deep breathing, and gentle coughing was from 10 to 25 cm. H_2O in most subjects, and this will be referred to later as the 'physiological pressure range'.

At the start of each experiment the resting pressures were recorded and a slight increase above the resting level was made to allow gentle filling of the duct system, which, once filled, was deemed for practical purposes to be indistensible during short periods of time. The flow into the patient in millilitres per minute was then observed at various pressures and the results recorded. Certain drugs were administered at times in most patients and some of their effects will be noted later. Pressures of perfusion were usually low at the beginning of each study and it was hoped in this way to minimize any spasm which might otherwise have been induced by sudden loading of the sphincteric muscle.

Several readings were taken at each chosen pressure with 5 cm. H_2O pressure differences in most subjects between groups of observations. Having recorded flow volumes at pressures up to 45 cm. H_2O, a series of readings was made on the return to resting pressure. Final pressure readings were made which seldom differed from the initial figures. The results were recorded and have been expressed in graphic form.

RESULTS

Sixteen patients were investigated of whom 6 had had sphincterotomies. The indications for sphincterotomy were: pancreatitis (1), post-cholecystectomy pain (1), and impacted stones in the lower end of the common duct (4).

The other patients had had no operation on the lower end of the duct and were assumed to be normal in their sphincteric responses. In this group there was a characteristic flow curve which was obtained with only minor variations in all these subjects (*Fig.* 25). The characteristic of this curve was an approximately exponential form with a noticeable step between the 15 and 20 cm. recordings. A rise in perfusion pressure of 5–10 cm. from the resting value led to a small increase in flow. However, once the step was reached the graph became linear, suggesting that some resistance was overcome at about 20 cm. pressure. It will, of course, be appreciated that the pressures of real interest are those in the physiological range of 15 cm. above the resting pressure.

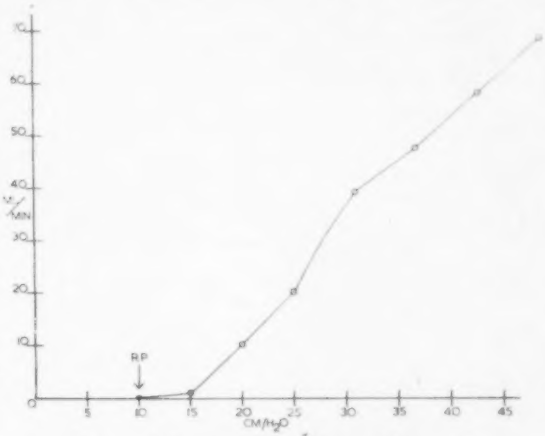


FIG. 25.—A flow curve obtained from studies on a 48-year-old woman 12 days after exploration of the common duct. The sphincter had not been sectioned. Note the resting pressure level (RP) and the change in direction of curve after the 15-cm. reading.

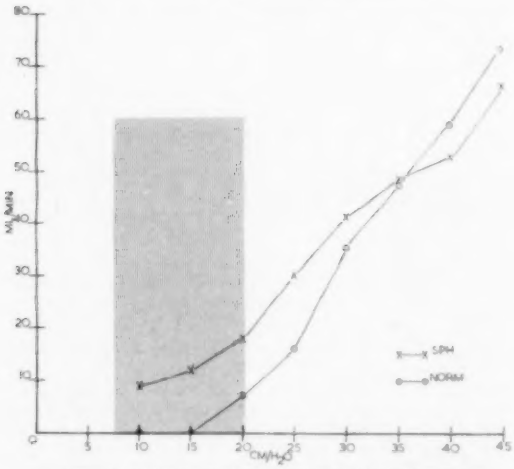


FIG. 26.—Flow curves from 2 patients with similar resting pressures. Both were taken 12 days after operation. Upper record (x – x) from a 49-year-old woman who had had a sphincterotomy. Lower record (o – o) from a 37-year-old woman who had had a simple exploration of the common duct. Note difference in flow behaviour, particularly in physiological pressure range (cross-hatched on graph).

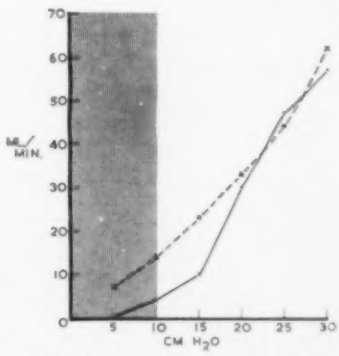


FIG. 27.—Mean flow curve from 16 studies from 10 normal subjects ('——') on graph, for comparison with mean values from 10 studies from 6 sphincterotomized patients (x - - - x). All pressures are reckoned from resting value, *not* absolute pressure. Physiological range shadowed. This shows increment of average flow by sphincterotomy.

The high flows observed at high pressures are of no significance in a system designed to cope with a daily flow of only 800–1200 ml. of bile.

When a patient after sphincterotomy was investigated in a similar way, a flow curve (*Fig.* 26) was drawn which differed markedly from that of the normal group. The main differences were the absence of a 'shoulder' and a markedly higher starting-point. Thus, within the physiological range, considerable flow was observed at low pressures and

this apparent augmentation could be contrasted with the findings in a patient of the normal group who had the same resting pressure. Outside the physiological range (shaded on the graph), the two curves appeared to converge. This has little significance except to show that, at very high perfusion pressures, the influence of the sphincter is overcome.

In order to draw a comparison between the two groups, rather than between individual subjects, a further graphic attempt has been made. This (*Fig.* 27) consists of the mean flows in ml./min. in 16 studies on 10 normal patients compared directly with the mean flows from 10 studies on the 6 sphincterotomized patients. Since their resting pressures varied, the individual resting pressure has been made the zero point of the pressure range. An arbitrary physiological pressure range of 10 cm. has been accepted. The mean flow curves of the two groups are comparable with the individual subjects' curves seen in *Figs.* 25, 26. The unbroken line of the normal group is seen to indicate no effective flow at 5 cm./H_2O above resting pressure while, at 10 cm./H_2O, the flow is only of the order of 5 ml. per minute. This is in direct contrast to the sphincterotomy group whose performance is shown by the broken line. Here there is a flow of 8 ml. at 5 cm./H_2O pressure, with a rise to 15 ml. with a further 5 cm. increase. Again it will be seen that as the physiological pressure range recedes, the curves come to meet each other, as was noted in *Fig.* 26.

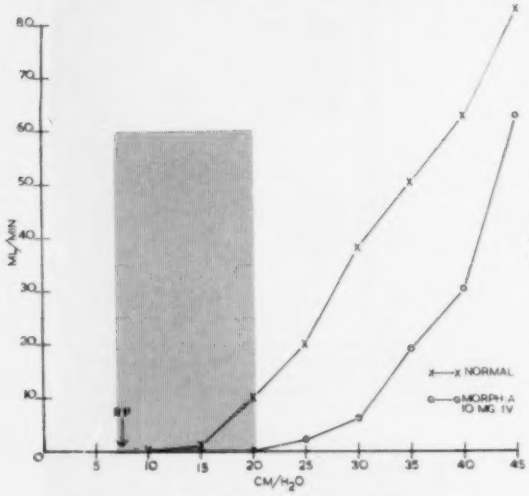


FIG. 28.—Flow curves obtained from a 44-year-old woman 13 days after exploration of common duct. First curve (x – x) before and second curve (o – o) after 10 mg. morphine intravenously. This shows very marked depression of flow, with abolition in physiological pressure range.

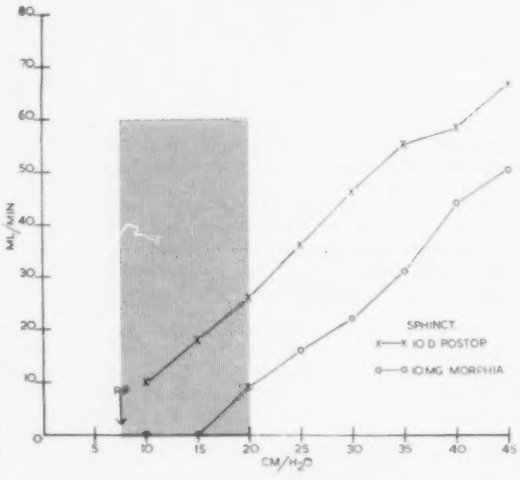


FIG. 29.—Flow curves obtained from a 61-year-old woman 12 days after sphincterotomy. This shows marked reduction in flow after 10 mg. morphine intravenously. Note, however, that some flow occurs in physiological pressure range (cf. *Fig.* 28).

Effect of Drugs.—In 12 patients a flow study was carried out under the standard conditions and then an intravenous dose of 10 mg. of morphine sulphate was given. After a lag of 10 min. to allow the effect of the drug to develop, a further flow curve was obtained. These experiments were performed on patients of both groups and the results are shown in *Figs.* 28, 29. In all subjects the resting pressures were unaffected by morphine and thus the flow curves of a subject before and after the drug could be compared on the same graph. The normal subjects gave the usual curve with small flows in the physiological range and the characteristic step in the 15–20 cm. range. After morphine was administered flow was profoundly depressed. On the graph, a shift to the right shows the abolition of flow in the normal range with the step transposed to the 30–35 cm. range.

After sphincterotomy, flow was seen (*Fig.* 29) to be depressed by morphine, but some drainage was still possible at physiological pressures. In fact, even with the spasm produced by 10 mg. of morphine the flow in a sphincterotomized patient was almost comparable with that of the normal patient without drugs. Some depression of flow was, however, seen in this group of subjects. It must be remembered that spasm is due to the contraction of all muscular elements of the duodenal wall, only part of which is affected by even the most ambitious sphincterotomy.

From all of these studies it was concluded that sphincterotomy has a useful function in the augmentation of flow in the human common bile-duct. The effects upon pancreatic flow have not been assessed though they may be inferred in those subjects where there is a common channel.

DISCUSSION

Since Oddi (1887) described the muscle of the lower end of the common duct, a number of investigators (Boydon, 1937, 1956; Schreiber, 1944; Sterling, 1952; Matsuno, 1993) have confirmed and extended his observations. The operation of transduodenal sphincterotomy advocated by Doubilet and Mulholland (1948, 1949) and by Doubilet in 1957 in the treatment of pancreatitis and pancreatic pseudocysts has given many satisfactory results.

Further applications of sphincterotomy are numerous. The removal of stones from the lower end of the common duct requires no further comment. It may well be that this operation has a place in the management of functional abnormalities of biliary drainage. These have been extensively discussed by Mallet-Guy and his colleagues (Mallet-Guy, Jeanjean, and Feroldi, 1945; Mallet-Guy, Lacour, Koppes, and Refussy, 1949), though the postulated syndrome of biliary dyskinesia has not yet won universal acceptance. Here, biliary drainage is deemed to be impaired by sphincteric hypertonicity and relief can be anticipated when the choledochoduodenal sluicegate is opened. There is a place for this operation in the relief of the post-cholecystectomy syndrome whether or not there is any residual cystic duct stump.

The anatomical basis of the operation is simple. It consists of an incision through the duodenal mucosa and oblique muscle cuff that surrounds the intramural part of the common biliary and pancreatic duct (Boyden, 1956; Hand, 1958). This lays open the terminal part of the common channel, allows the pancreatic duct to open directly into the duodenum, obviates the possibility of biliary reflux up the pancreatic duct, and reduces the pressure against which the two ducts must empty.

Since the common duct and common pancreaticobiliary channel pass through the duodenal muscular wall before they come to lie ensheathed in smooth muscle in the submucosa, sphincterotomy carried out from the duodenal lumen can with safety only section some of the muscular fibres. An overenthusiastic operator runs the risk of damaging the duodenal wall and hence inducing fistulation. As this is then only an incomplete operation, it has seemed pertinent to settle the question of whether there is any real change in the drainage of the duct.

The effect of sphincterotomy has been investigated by pressure studies in cats by Eisman and his colleagues (1959). Their conclusions in the experimental animal are gloomier than are expected on clinical grounds in human subjects. According to their results, the effective duration of effect is short and they suggest that re-stenosis and fibrosis are inevitable. Their studies in animals involve a rather longer follow-up than is possible in human subjects. Certainly in the present series, no diminution in flow was noted up to one month from operation in our subjects.

Numerous authors have previously noted the marked sphincteric spasm caused by drugs (Butsch, McGowan, and Walters, 1936; Menguy, Hallenbeck, Bollman, and Grindley, 1958). The observation that induced spasm cannot be abolished entirely by sphincterotomy does not detract from the value of the operation, but accentuates the knowledge that only a part of the choledochoduodenal barrier can be breached at operation.

The present studies of flow are complementary to previous investigations where the emphasis was upon pressure changes during perfusion, such as those of Parry and others (1955), Doubilet and Colp (1937), and Newman and Northup (1957). It is felt, however, that actual flow measurements give more indication than do pressure recordings, which only hint indirectly at the combined effects of flow and resistance that lead to pressure alterations.

CONCLUSION

Transduodenal sphincterotomy is often carried out to augment the flow of bile into the duodenum. Its effects have been investigated by comparing flow characteristics in two groups of patients who have had biliary operations. The patients who have undergone sphincterotomy have a significantly different flow curve from the normal group. Comparison of the results suggests that sphincterotomy augments flow in the physiological pressure range.

This experimental work was carried out during an appointment in the Department of Surgical Studies, Middlesex Hospital. The author is grateful to Mr. D. H. Patey and Mr. L. P. LeQuesne for permission to investigate their patients and for their advice and encouragement. The apparatus was made in the workshop of the Institute of Clinical Research, the Middlesex Hospital, and illustrations were prepared in the Department of Medical Illustration.

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PRIMARY CARCINOMA OF THE EXTRAHEPATIC BILE-DUCTS

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PRIMARY tumours of the extrahepatic biliary ducts are commonly regarded as localized lesions; hope that they might surrender readily to advances in surgical technique has, however, not so far been fulfilled. The results of attempts at radical removal, no matter how favourable the circumstances might seem at the time, have proved to be uniformly bad. The adverse factors to be considered include difficulty in making a confident diagnosis, early spread to adjacent vital structures, and the technical limitations of surgery in this region. Tumours at the porta hepatis are, in the present state of our knowledge, incurable from the outset. If we consider those more distally placed, the problem, as with malignancy elsewhere, resolves itself into need for earlier diagnosis and further investigation of the biological behaviour of these growths.

MATERIAL

This is a study of 62 patients admitted to the Western Infirmary, Glasgow, during the 20-year period, 1939–58. Following the custom of other writers, cases with ampullary and intrahepatic growths are omitted from the series, since in each of these groups it is often impossible to establish with certainty the precise site of origin of the primary tumour. We have included patients with tumour of the cystic duct. Earlier authors, such as Rolleston and McNee (1929) and Stewart, Lieber, and Morgan (1940), regarded these as arising in the gall-bladder, but more recently they have come to be accepted as tumours of the extrahepatic biliary ducts. The diagnosis of carcinoma was confirmed histologically in 54 cases; in a further 8 cases no histological examination of the tumour was made, but the findings at operation and the subsequent course of the disease were characteristic. Biochemical data are considered only during the last five years of the period covered by the study since it is only recently that hepatic function tests have been standardized. Reference will also be made to the value of radiological diagnosis.

PATHOLOGY

The diagnosis of carcinoma of the extrahepatic bile-ducts was confirmed histologically in 54 cases. Adequate records of gross and microscopical data were available in all of these, while histological sections were personally reviewed (J. G.) in 33 of the acceptable cases.

In surgical biopsy material the pathologist relies greatly on the surgeon's description of the gross anatomy and his selection of suitable tissue for examination. Tumours arising from the various structures in the region of the bile-ducts may present similar or identical histological appearances. A firm diagnosis was made in 11 cases where a biopsy of the affected duct was taken. A further 5 biopsies of liver showed tumour compatible with origin in bile-duct. In 1 case liver biopsy showed only subacute cholangitis with evidence of obstruction, but the presence of a carcinoma was confirmed at subsequent necropsy. In the remaining cases histological confirmation was obtained at necropsy.

Sex and Age.—There were 27 men and 35 women. Our sex ratio (3 : 4) is not in accordance with the findings of Sako and others (1957), who found it to be in the proportion of 3 men to 2 women in 433 cases collected from the world literature during the period 1935 to 1954. Most of our cases were in the 50–70-age-group, which is similar to other published reports.

Incidence.—Sako, Seitzinger, and Garside (1957) found in their extensive review of the literature a necropsy incidence varying from 0·012 to 0·458 per cent, while their own series showed an incidence of 0·38 per cent. The present series of 37 necropsies shows an incidence of 0·05 per cent of all the necropsies over the same period, with carcinoma of the extrahepatic biliary tract at least as common as either carcinoma of the gall-bladder or pancreas, and about three times as frequent as carcinoma of the ampulla of Vater.

Aetiology.—There is no evidence to suggest a relationship between cholelithiasis and carcinoma of the extrahepatic bile-ducts such as probably obtains in carcinoma of the gall-bladder. The reported incidence of gall-stones in cases of carcinoma of the extrahepatic bile-ducts varies considerably (Stewart and others (1940), 20·2 per cent; Sako and others (1957), 38·7 per cent; and Neibling, Dockerty, and Waugh (1949), 57 per cent), but the average of these figures (33·6 per cent) approximates closely to that of 32·9 per cent found by Crump (1931) in his ordinary necropsy series covering the same age-groups as the above published reports. The present series shows an incidence of 33·9 per cent.

Suggested predisposing causes include malignant transformation of a simple duct papilloma (Dick, 1939), chronic infestation with *Lamblia intestinalis* (Grott, 1938), and the action of endogenous and exogenous carcinogens, excreted by the liver and concentrated in the bile. It is known that bile acids are related chemically to the carcinogenic hydrocarbons of the benzanthracene group, and methylcholanthrene has been synthesized from both desoxycholic acid and cholic acid; Kennaway (cited by Willis, 1960) has shown that desoxycholic acid, a normal component of bile, can produce sarcoma in mice.

Table I.—NECROPSY FIGURES FOR CARCINOMA OF EXTRAHEPATIC BILIARY DUCTS, 1939–58

Macroscopic Type of Tumour	*Number*	*Percentage*
Annular stenoses	15	40·5
Diffuse thickenings of bile-duct	5	13·5
Papillary tumours	2	5·4
Small nodular tumours	9	24·9
Bulky ill-defined tumours	5	13·5
Unclassified	1	2·7
Total	37	

Structure of Tumour.—That the gross form of the tumour is variable is shown in *Table I*. The affected duct may be partially or completely occluded

by the formation of an annular stricture or by a small nodule or papillary tumour encroaching upon the lumen. The anatomy of the duct system is commonly grossly distorted by the bulky ill-defined type of neoplasm. Mucosal œdema and mobile papillary tumours may produce intermittent occlusion, while invasion of muscle and involvement of motor nerve innervation may result in reflex spasm and obstruction to the biliary flow.

Site of the Tumour.—In necropsy specimens it is relatively easy to determine the site of origin of the tumour except in the case of diffuse scirrhous

Table II.—Site Distribution of Tumours

Site of Tumour	*Number of Cases*	*Cholelithiasis present*
One branch of common hepatic duct	1	—
Bifurcation of common hepatic duct	3	—
Common hepatic duct	16	5
Cystic duct	4	4
Tripartite junction	12	9
Common bile-duct	26	3
Total	62	21

and bulky cellular neoplasms. Willis (1942) suggests that such large tumours may arise over a wide area as a result of multicentric origin. Well-localized tumours were most commonly found in the common bile-duct, and were usually small nodular adenocarcinomata or annular strictures. The site distribution in this series is given in *Table II*.

Microscopical Appearances.—Sako and others (1957) stress the confusion in the nomenclature of these neoplasms and we therefore adhere to the simple classification shown in *Table III*, which may be further subdivided into tumours of low, average, and

Table III.—Microscopical Types of Tumour in 1939–58 Necropsy Cases of Carcinoma of Extrahepatic Bile-ducts

Microscopic Type	*Number*	*Percentage*
Adenocarcinoma	18	48·6
Infiltrating scirrhous carcinoma	13	35·1
Papillary adenocarcinoma	3	8·1
Anaplastic carcinoma	2	5·4
Unclassified	1	2·7
Total	37	

high grades of malignancy on the basis of cellular differentiation, although even with growths of apparent low malignancy the prognosis is uniformly bad. Cellular adenocarcinoma and infiltrating scirrhous carcinoma form the bulk of the tumours, but some growths show both features. The acini show great variation in size in the two types, the scirrhous type of growth usually having numerous small acini, while in the more cellular adenocarcinomata the acini are large and often show slight papillary change. Mucin production is usually present, but varies in amount, and in 1 case a tumour obstructing the common bile-duct showed an unusually frondose appearance with considerable production of mucus and could be regarded as a cystadenocarcinoma (*Fig.* 30). Squamous metaplasia was observed in 5 cases, all of which showed poor differentiation and a high grade of malignancy. Mitotic division is not frequent in the scirrhous tumours and less florid adenocarcinomata, but in the poorly differentiated neoplasms and in the two anaplastic tumours mitoses were frequent and the cells were pleomorphic.

Spread of Tumour.—Local infiltration of the wall of the affected duct is the commonest microscopical evidence of spread. Neoplastic cells permeated regional lymphatics in just over 50 per cent of cases, but blood-vessel invasion is rare. In the 33 cases with histological sections available for personal review, permeation of the perineural lymphatics was found in 39·3 per cent. Masuda (1935)

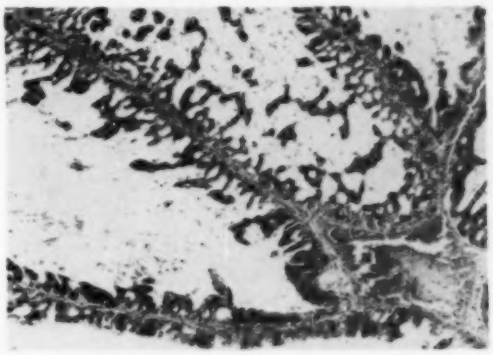

Fig. 30.—Low-power view of papillary cystadenocarcinoma of common bile-duct, showing finely frondose pattern. H. and E. (× 32·5.)

and Neibling and others (1949) also commonly found nerve invasion in their series.

Lymphatic spread involved chiefly the hepatic chain of nodes, the cystic node, and pancreaticosplenic group in order of frequency. In 1 case the para-aortic nodes were invaded by a highly anaplastic tumour, while the omentum, mesentery, and peritoneum were involved in 4 cases. The pancreas was most commonly affected by direct extension from tumours situated just above the ampulla.

Hepatic metastases were found in 37·8 per cent and showed three main forms: as multiple scattered nodules often with central necrosis and umbilication near the surface of the organ; as a large mass at the porta hepatis; or, occasionally, as massive involvement of one or both lobes of the liver.

Both ovaries were almost completely replaced by gelatinous tumour tissue in a female aged 45 years who had a poorly differentiated tumour of the common bile-duct. Histological examination of the ovaries showed invasion with a poorly differentiated carcinoma often showing signet-ring cells with production of mucin, but without the characteristic stromal reaction found in the classical Krukenberg tumour. No other primary tumour was found in this case. Extra-abdominal spread was not seen in the present series, but Willis (1960) cites 2 cases of pulmonary metastases and Sako and others (1957) found metastases to be present in a single cervical lymph-node in 1 case.

Coexistence of Two Primary Tumours.—In this series there were 3 cases of coexisting biliary and non-biliary primary tumours; 2 were primary gastric carcinomata which were regarded by the late Professor J. Shaw Dunn as separate primary growths, and the third a carcinoma of the colon (*Figs.* 31, 32). In a further case of a female aged 63 years a carcinoma of the sigmoid colon had been removed but

recurred locally two years after resection. At necropsy it was noted that there were now metastases in the liver, but in addition there was also a carcinoma of the common bile-duct; histological examination of

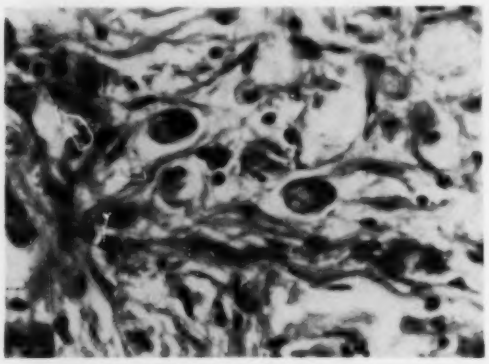

FIG. 31.—High-power view of a diffuse primary tumour of stomach wall to show characteristic signet-ring cell infiltration. H. and E. (× 420.)

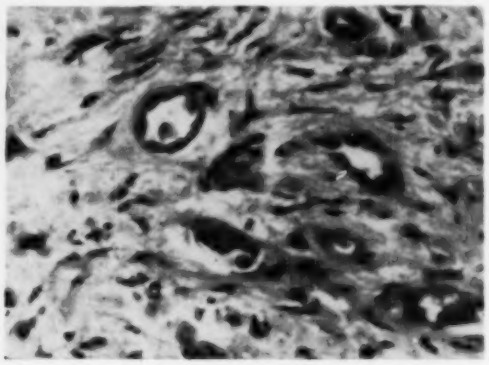

FIG. 32.—High-power view of coexisting primary tumour of common bile-duct in same case as *Fig.* 31. The tumour here is a scirrhous carcinoma of small acinar type. H. and E. (× 420.)

the liver secondaries suggested that they had arisen from the bile-duct tumour rather than colon.

Associated Liver Pathology.—Apart from tumour invasion the liver frequently showed changes resulting from prolonged obstruction, i.e., gross bile staining and distension of the intrahepatic bile-ducts. Ascending cholangitis with abscess formation was occasionally seen and varying degrees of hepatic necrosis were often present.

CLINICAL FEATURES

It is of interest that 11 patients were admitted to medical wards and died there, while 51 patients came to the surgical side. It is fair to state that the symptoms of the 'medical' group were bizarre, e.g., pains in the joints and back; only 1 complained of abdominal pain. Weakness and loss of weight were common; 2 died of coronary artery thrombosis before any lesion of the biliary tract was suspected. Five of this group were not jaundiced. The following are the main clinical findings in the total group of 62 patients.

Jaundice was present in 53 cases (85·5 per cent). Its duration before admission to hospital varied within wide limits. There were only 13 patients seen in the early phase, i.e., within three weeks of onset; 38 patients had been jaundiced for two to four months, and 2 others for as long as six and ten months respectively. The jaundice was progressive and unremitting in most of the cases, but in 14 patients (22·6 per cent) it fluctuated in intensity; of these, there were 8 in whom the skin cleared completely for varying periods. One patient who had been jaundiced on six occasions within the space of ten months ultimately became fit for duodenopancreatectomy. As suggested above, the variation in the intensity of the jaundice can only be explained by change in the degree of obstruction produced by the tumour itself, by spasm of the duct, or on the basis of associated inflammation, since in no instance were there gall-stones in the common bile-duct, although 4 patients suffered from cholelithiasis. Others have commented on this very misleading clinical sign—Kuwayti, Baggenstoss, Stauffer, and Priestley (1957), for example, noted fluctuation in the degree of jaundice in as many as 60 per cent of their series with biochemical confirmation.

Abdominal Pain was noted in 46 patients (74·2 per cent); by 6 patients it was described as a vague discomfort, by 22 as a gnawing pain, and by 18 as an intense colic. The most commonly affected areas were the epigastrium and the right subcostal region; less often the pain was central abdominal, and occasionally in the left subcostal and thoracolumbar regions. Indeed, the clinical picture, taking into account a coexisting jaundice, could scarcely be distinguished from that of obstruction of the biliary system due to stone. One patient illustrates this point: he suffered three separate bouts of acute pain over a period of three months, followed on each occasion by jaundice which cleared between attacks. His lesion proved to be a tumour situated at the junction of the cystic and common ducts, unassociated with stones. A further confusing aspect was a history of intermittent epigastric pain of varying degree for two or three years before certain patients came under observation. There were 7 patients in this category; in 3 of these cholelithiasis might have been the cause, but in the remainder there was no obvious explanation.

The time incidence of pain and jaundice was studied in 39 cases. The pain developed before the jaundice in 31 patients and afterwards in 8; in 14 cases the onset of jaundice was delayed by a month or more, and it is interesting to note that the clinical clerks responsible for these particulars referred to the jaundice as 'painless'. This may have been strictly true in point of time, but conveys a misguided impression that these tumours are not at some time associated with pain. In 1 case intense colic and nausea of twelve hours' duration occurred three months before jaundice appeared; significantly, a weight loss of 2 st. had developed during that period.

The *cause* of pain has been ascribed to the following:—

1. *Gall-stones*: 21 patients suffered from gall-stones, but of these only 11 had pain; their stones were confined to the gall-bladder.

2. *Distension* of the biliary system proximal to the site of obstruction by tumour.

3. *Stretching* of the liver capsule.

4. *Local nerve invasion* by tumour (Neibling and others, 1949; Kuwayti and others, 1957).

Loss of Weight was almost as frequent as pain, the number of our patients so affected being 45 (72·6 per cent). This diagnostic point requires emphasis, especially in those suffering pain of the kind suggesting stones in the ducts rather than tumour. Weight-loss is generally believed to be due principally to loss of appetite and to nausea induced by back pressure on the liver, rather than due to a specific cachexia of neoplastic origin (Sako and others, 1957).

Anorexia and Nausea were recorded in 31 patients (50 per cent), but this might well be an underestimate. *Vomiting* occurred only in patients with severe pain. Only 8 patients complained of *flatulence* and a sense of fullness, this being less common than anticipated. *Rigors* were very infrequent and occurred in only 2 patients. This is in striking contrast to obstruction by stone, where chills, fever, and occasional rigors occur frequently.

Hepatic Enlargement was present in 40 patients (64·5 per cent), and a mass which might have been a tumour or a distended gall-bladder was palpated in 15 (24·2 per cent). The law of Courvoisier applies to this form of malignancy only when the site of the tumour is distal to the entry of the cystic duct into the common bile-duct. A more reliable pointer is enlargement of the liver.

BIOCHEMICAL INVESTIGATIONS

Where the jaundice is clearly and unequivocally obstructive in nature chemical analyses are not strictly necessary for the management of the patient. Many of our cases fell into this category and no biochemical estimations were carried out. In carcinoma of the extrahepatic biliary ducts, the usual findings are: (1) Increase in the serum-bilirubin, which may be intermittent in the early stage; (2) Increased alkaline phosphatase activity in the serum; (3) Normal serum flocculation tests; (4) Presence of bilirubin and absence of urobilinogen in the urine in the later stages; and (5) A moderate increase in both the serum glutamic-oxalacetic transaminase and the serum glutamic-pyruvic transaminase activities—the activity of the latter being always greater than that of the former. Other common findings, especially in cases of long-standing jaundice, are: (*a*) A steady decrease in serum albumin concentration; (*b*) An increased prothrombin time which returns to normal a few hours after injection of vitamin K; and (*c*) Increased bromsulphthalein retention. This last test should not be employed if the patient is jaundiced, with a serum-bilirubin level greater than 3·0 mg. per 100 ml. Only exceptionally is it necessary to carry out more than a few investigations, the most important analyses being those of the serum-bilirubin concentration and the alkaline phosphatase activity.

Table IV.—Biochemical Details of *Case* H. S. (Male, aged 60 years)

Date	Bilirubin (mg. per 100 ml. serum)	Alkaline Phosphatase (King-Armstrong units per 100 ml.)	Thymol Turbidity and Flocculation*	Albumin (g. per 100 ml.)	Total Globulins (g. per 100 ml.)
April 4, 1958	First appearance of jaundice				
April 18, 1958	First admission				
April 18, 1958	19·0	16	1–0	4·0	2·1
April 23, 1958	24·0	17	1–0	4·3	1·8
April 25, 1958	Laparotomy. No biliary obstruction found. Condition believed to be infective hepatitis. No biopsy obtained				
April 28, 1958	27·0	16	0–0	3·5	1·8
May 3, 1958	24·6	16	1–0	3·2	2·1
May 6, 1958	23·0	16	0–0	3·2	2·1
May 9, 1958	24·0	15	1–0	3·4	1·9
May 12, 1958	20·8	18	1–0	3·2	1·6
May 19, 1958	16·0	15	1–0	2·7	2·1
May 26, 1958	17·2	20	1–0	2·7	2·1
June 3, 1958	15·4	24	1–0	2·8	2·4
June 4, 1958	Discharged home				
Sept. 2, 1958	Second admission				
Sept. 3, 1958	24·0	39	1–0	3·2	2·0
Sept. 8, 1958	Laparotomy. Carcinoma of the hepatic ducts, believed to have started in the left duct and now beginning to invade the proximal end of the common bile-duct				
Sept. 19, 1958	26·0	53	0–0	3·0	1·8
Oct. 3, 1958	Patient died				

* First figure, turbidity in arbitrary units (normal 0–2 units); second figure, degree of flocculation (normal zero).

In the present series the serum-bilirubin concentration was estimated pre-operatively in 11 cases, and was increased in all. The upper normal limit is generally taken to be 1·0 mg. per 100 ml.; in these 11 cases the pre-operative level lay between 2·0 and 38·8 mg. per 100 ml. In that case, where the serum-bilirubin was 2·0 mg. per 100 ml., the serum alkaline phosphatase was 47 King-Armstrong units per 100 ml.—a clear indication of an impending obstructive jaundice.

The normal serum alkaline phosphatase activity in adults lies in the range 4–12 King-Armstrong units per 100 ml. In the absence of any bone disease involving osteoblastic activity, a serum alkaline phosphatase activity greater than 30 King-Armstrong units per 100 ml. (combined with an increased serum-bilirubin concentration) is practically diagnostic of

obstructive jaundice. In all of our 11 cases investigated biochemically, the serum alkaline phosphatase activity was increased. Two pre-operative values were comparatively low (16 and 21 King-Armstrong units per 100 ml.), but in the same specimens the serum-bilirubin concentrations were 19·0 mg. and 24·0 mg. per 100 ml. respectively. In the remaining 9 cases the serum alkaline phosphatase activity ranged from 32 to 83 King-Armstrong units per 100 ml. before operation.

In our series the most interesting, from the biochemical aspect, was a case of initially unclassified jaundice in which the clinical findings were unusual. The main features are tabulated in *Table IV*.

The interesting features in the biochemistry of this case are:—

1. The relatively low alkaline phosphatase activity on admission, combined with a relatively high bilirubin concentration.

2. The marked, but irregular, decrease in the serum-bilirubin concentration after the first laparotomy, although the patient at that time must have had a hepatic duct carcinoma.

3. The serum alkaline phosphatase activity was not significantly high until the second admission.

These seemingly paradoxical findings may be explained on the grounds that the carcinoma originated in the left hepatic duct, while the right duct and the right lobe of the liver were not involved until later. The irregular decrease in the serum albumin concentration was most probably due to progressive dysfunction of the liver, the site of serum albumin formation. This type of case, although of great biochemical interest, presents an insoluble surgical problem.

RADIOLOGICAL INVESTIGATIONS

Until recently, no information could be obtained from attempts at cholecystography and cholangiography in the jaundiced patient, since the medium was not sufficiently concentrated to cast a shadow. The procedure was considered dangerous since an additional burden was thereby cast on an already damaged liver. The newer oral and intravenous preparations, such as telepaque and biligrafin, do not appear to damage the liver, but are unfortunately of little value in outlining the bile-ducts when severe jaundice is present. Wise and O'Brien (1956) have shown that when the serum-bilirubin level exceeds 4 mg. per 100 ml. it is improbable that the bile-ducts or the gall-bladder will be demonstrated satisfactorily by the use of biligrafin. The studies of Stenhouse (1956, 1958) confirm these findings but show that in elucidating certain difficult cases biligrafin and telepaque may be used in combination. In our series no positive assistance was derived from radiological studies.

TREATMENT AND RESULTS

The ideal case for radical surgery has a localized lesion well away from the porta hepatis and an ample hepatic reserve. In the experience of ourselves and others these criteria are seldom realized. The various forms of treatment employed in our series are summarized with the results in *Table V*.

Table V.—Summary of Treatment and Results in 62 Cases of Carcinoma of Extrahepatic Bile-ducts

Form of Treatment	No. of Cases	Average Survival Period from Onset of Jaundice	Post-operative Survival in Radically Treated Group	
			Up to 2 weeks	Months
Conservative:—				
1. No operation	22	3·4 mth. (Longest—8 mth.)		
2. Laparotomy only	14			
Palliative:—				
1. Anastomosis of gall-bladder to stomach or bowel	5	5·5 mth. (Longest—18 mth.)		
2. Cholecystostomy	2			
3. Choledochostomy and bouginage	7			
Radical:—				
1. Cholecystectomy	3		2 cases	One lived 7 mth.
2. Resection of supraduodenal segment	5		1 case	Three lived 4, 20, and 33 mth. respectively and 1 case still alive after 38 mth.
3. Duodenopancreatectomy	4		2 cases	Two lived 4 and 9 mth. respectively

We would emphasize that 36 patients (58·1 per cent) were unfit for even palliation and that 22 died without a laparotomy (including the 11 'medical' cases).

Palliative Relief of the jaundice was undertaken in 14 patients (22·5 per cent). This was achieved: (1) by anastomosis of gall-bladder to stomach, duodenum, or jejunum; or (2) by creating an external fistula, thus draining the gall-bladder or common bile-duct to the surface. The latter was a necessary makeshift procedure following upon the unexpected discovery of a tumour. In some cases bouginage was necessary, either as an investigative measure or to provide space for an indwelling catheter. It is of interest to note that Pack (1958) advises against the use of the gall-bladder for bypassing the lesion since the cystic duct is liable to become occluded at an early date by tumour spread. He advocates anastomosis of the proximal segment of the common hepatic duct to a jejunal loop; if there is not a sufficient length of the former he

recommends the Longmire procedure in which the left main intrahepatic duct is used for anastomosis. This latter, in our opinion, is justifiable in high benign strictures but not as a palliative procedure for a malignant lesion.

Radical Surgery was undertaken in 12 cases (19·4 per cent). *Cholecystectomy* was carried out in 3 cases with tumours of the cystic duct. This operation was certainly inadequate since the longest survival was only for 7 months, but in each case the true nature of the lesion was not fully recognized at operation. *Resection* of tumours in the supraduodenal segment plus cholecystectomy was carried out in 5 patients and continuity restored by anastomosing the common hepatic duct to the jejunum, utilizing a *Roux-en-Y* loop. Finally, 4 cases with tumours in the region of the head of the pancreas were treated by *pancreaticoduodenectomy*.

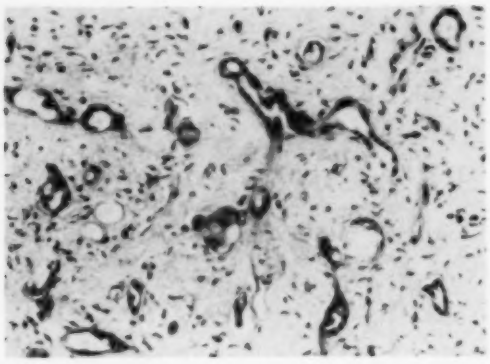

FIG. 33.—Medium-power view of tumour of common bile-duct in a male aged 47 years who is still alive and well 38 months after operation. This is a scirrhous carcinoma of small acinar type. H. and E. (× 168·5.)

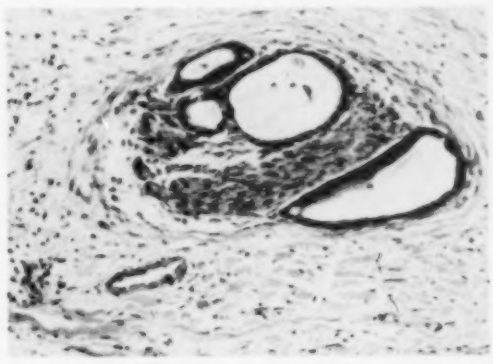

FIG. 34.—Low-power view of another field from the same tumour as *Fig.* 33 to show invasion of perineural lymphatics. The tumour here is showing a more columnar celled adenocarcinomatous appearance. H. and E. (× 120.)

The assessment of the results of treatment in terms of survival period is not easy. In those where palliation or expectant treatment only can be considered, it is customary to calculate from the onset of jaundice rather than other symptoms such as pain, whereas in the radically treated group only the post-operative survival time is taken into account. As we have shown, the jaundice may be intermittent and was, indeed, absent in 9 cases. Further, pain, when present, often precedes jaundice and might therefore provide a more reliable index of the duration of the disease. Nevertheless, we conform with custom and take the onset of jaundice as a basis of calculation.

The average survival period in the group treated expectantly was 3·4 months, the longest period being 8·0 months. In the palliative group it was 5·5 months, the longest period being 18 months. Goldenberg (1953), however, reports a case with 6 years' survival following a simple short-circuit procedure.

In those subjected to radical surgery only post-operative survival periods were considered; 5 died within 2 weeks following the operation for the following reasons: hæmorrhage, anastomotic leak, liver necrosis due to hepatic artery damage, and hepatic coma. For comparison we again quote Goldenberg, 9 of whose series were treated by radical surgery; 6 died in less than 6 months and the remainder after 13, 25, and 36 months, respectively. The survival periods in our series are given in *Table V*; these show that results following resection of the middle zone are better than those of duodenopancreatectomy. Three of the former group lived beyond a year, i.e., 1 for 20 months, another for 33 months, and 1 is still alive and working after 38 months (operation by D. B. B.). The histological features of the excised tumour in this last case are shown in *Figs.* 33, 34.

The figures speak for themselves: we have little more than palliative relief to offer these patients. They belie the impression that biliary carcinomata are sometimes localized and recall the poor prognosis of carcinoma of the pancreas. Nevertheless, we have shown that worthwhile survival can occasionally be achieved. Clinical experience suggests that better results might be obtained by the adoption of an earlier and more aggressive surgical approach whenever obstructive jaundice is suspected on clinical or biochemical grounds.

SUMMARY

A total of 62 cases of primary carcinoma of the extrahepatic biliary ducts admitted during the 20-year period 1939–58 to the Western Infirmary, Glasgow, are reviewed. There were 27 men and 35 women and the majority of the patients were in the 50–70-year age-group. The pathological and biochemical aspects of the condition are discussed. Biochemistry affords great help in the diagnosis of this condition, but to date the results of radiological diagnosis have been disappointing. Half of the cases were beyond surgical aid when first seen; 1 in 4 was fit only for palliative relief of jaundice, and only 1 in 5 of the cases was resectable. The longest survival period for conservative treatment was 8 months; after palliative operation 18 months; following radical surgery 1 patient is alive and well after 38 months. A plea is made for earlier resort to surgery whenever obstructive jaundice is suspected.

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A CLINICAL APPROACH TO AN ANALYSIS AND TREATMENT OF POST-GASTRECTOMY SYNDROMES

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ABOUT 30,000 partial gastrectomy operations for peptic ulcer are carried out in Great Britain every year, and there is general agreement amongst the major centres concerning results. Thus Brookes, Waterhouse, and Thorn (1960), analysing the 955 patients treated by the Surgical Professorial Unit in Birmingham up to 1955, of which 79 had then died, 50 as an immediate or delayed result of operation, 29 subsequently from unrelated cancer, showed that the over-all mortality was 3·8 per cent (1·8 per cent under the age of 50 years; 14 per cent over the age of 65 years). Of the remaining 876, the number available for assessment was 826 (94·3 per cent): 66 per cent were, to all intents and purposes, cured; 22·6 per cent were greatly improved and glad that they had had the operation, being able to do everything they wanted to but still having to take precautions regarding avoiding certain articles of diet, or taking some antacid from time to time; and 12 per cent were failures. It is with this latter group that this paper is especially concerned. Even these may further be subdivided into those with fairly clear-cut symptom-patterns, and those with vague complaints not typical of anything particular. Thus the Birmingham series contained 17 cases of afferent loop syndrome, 15 of stomal ulcer, 3 of steatorrhœa, and 2 of dumping syndrome: the remainder were vague and varied, some now known to result from a belated onset of B_{12} deficiency and anæmia; some just psychologically unstable so far as pain or discomfort are concerned.

In view of the markedly altered anatomy that gastrectomy brings about—in the Billroth I type, with or without vagotomy, the stomach reservoir being reduced and emptying into the duodenum without sphincter control; in the Billroth II type, with or without vagotomy, the reservoir again being reduced and emptying direct into the jejunum, also without sphincter control—and the altered physiology that must result in consequence of altered enzymes, *p*H, bacteria, and peristalsis, it is perhaps surprising that about 70 per cent seem to have no ill effects whatsoever.

My interest in post-gastrectomy syndromes was enhanced when, as a result of a paper I published in 1952 concerning cases of loop-the-loop post-gastrectomy obstruction (Peterson's hernia, 1900), I received letters from all over the world recounting other patterns of similar herniations. One's reading and one's own problems as revealed by follow-up clinics, together with cases referred by colleagues, lead to a good deal of new thought and explanation which I now recount here.

Although Birmingham contributes her share of failures I must stress that not all the cases referred to in this paper come from our own series, but have either been referred from other hospitals, or have been culled from literature.

The patterns of discomfort complained of are many. Some are precise and constant, others are vague and variable. Some result from mechanical causes, others from metabolic, and, of course, mechanical factors may lead to metabolic disorders. It has also to be accepted that not all people are alike inside any more than they are externally; for instance, it has been shown that the richness of the oxyntic-cell carpet of the stomach varies from patient to patient—may this be related to any tendency to the development of stomal ulcer? Paulley (1954), Shiner and Doniach (1958), and others have demonstrated the degenerative process in the upper jejunal mucosa, a blunting of villi, that accompanies malabsorption states, and it is found in post-gastrectomy steatorrhœa too—was this state present before the operation, causing no more than a subclinical disturbance of fat metabolism, or does it result from the altered anatomy and consequent changed physiology brought about by the operation, the latter

triggering off, so to speak, an aggravation leading to steatorrhœa?

Some patients get their discomforts forthwith or as soon as they return to work, whilst others have several years of perfect health before developing their troubles. I suggest that the most practical way of classifying these failures is into (1) those with immediate trouble, and (2) those with delayed trouble.

FIG. 35.—Little stomach.

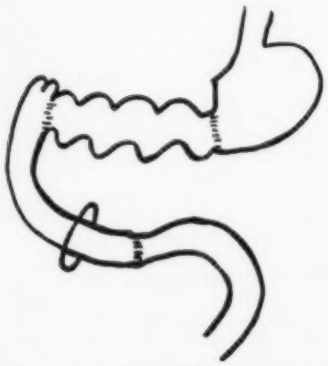

FIG. 37.—Enlargement of stomach reservoir by jejunal loop—Henley loop.

1. Immediate.—

a. First Few Weeks.—Many patients at first lack confidence and have a feeling of insecurity on first going home, but this soon improves with reassurance and a little guidance regarding indigestible foods, too bulky meals, or drinks with meals. It is for this reason that one should never attempt to assess the results of operations for peptic ulcer during the first year. It is during these first few weeks, too, that patients psychologically unsuited to surgery reveal themselves. Patients describing their symptoms in exaggerated and dramatic terms are better treated by other means, since, even if cured of their dyspepsia, they will probably complain of their wound.

FIG. 36.—Balloon measurement of little stomach.

FIG. 38.—Radiograph of an enlarged reservoir.

b. Little Stomach Syndrome.—Some patients continue to find that they cannot eat as much as other members of the family, and that beyond a certain amount they feel full and uncomfortable. They learn to content themselves with smaller meals; but those not sufficiently alert do not realize that they should increase the frequency of their meals to five or six

each day and, in consequence, lose weight and energy.

Duncan (1955), whilst working on the Unit, measured the capacity of stomach reservoirs following gastrectomy by using a potato–barium mixture, and found that anything less than about 250 c.c. tended to be associated with these symptoms of early fullness (*Fig.* 35). He further confirmed this by balloon studies (*Fig.* 36). If in a stable individual simple measures do not relieve the situation, it can

FIG. 39.—Intestinal hurry.

be remedied by enlarging the stomach reservoir by the interposition of a 15–20 cm. loop of jejunum, isoperistaltically placed, and with vascular pedicle intact, first described by Henley (1952), though practised here too, converting to a Billroth I and adding vagotomy to minimize the risk of anastomotic ulcer (*Fig.* 37); and the results are good (*Fig.* 38). The little stomach can initiate other symptoms too, such as are described later.

c. Intestinal Hurry.—Some patients, though feeling very much better, and relieved of their ulcer pain, state that their bowels move more frequently than hitherto, and that the stools tend to be looser, though not amounting to inconvenience; some, pointing to the right iliac fossa, say that they feel as if their food had reached that region within half an hour of taking it, and X-ray studies show that this is true (*Fig.* 39). If nutrition is good there is no need to do anything. Probanthine helps some of those worried by the symptom.

d. Steatorrhœa.—Another group of patients complain more definitely of diarrhœa, with the passage of pale, offensive stools that float on water, and on investigation this proves to be due to fat. A considerable amount of work has emerged from this School on the subject of steatorrhœa, idiopathic as well as that resulting from sprue, malabsorption, pancreatic disease, as also that following partial gastrectomy. Twelve years ago Brain, then with this Unit, made a study of the results of total gastrectomy for cancer and, in 2 cases, for hypertrophic gastritis with repeated hæmorrhages, concentrating particularly on the nutritional disturbances that follow in a high proportion of cases of total gastrectomy (Brain and Stammers, 1951). He found that fat metabolism was seriously disturbed, and evolved the theory of pancreatico-cibal asynchrony (1953), believing that as a consequence of altered anatomy, bile and pancreatic secretions were stimulated too late for them to mix with food conducted directly into the upper jejunum.

Gobbel, Shoulders, and Main (1960) have studied fat loss in stools following the different forms of partial gastrectomy, and give the following interesting figures:—

Normal	=	2·2 per cent
Polya without vagotomy	=	18·8 per cent
Polya with vagotomy	=	15·7 per cent
Billroth I without vagotomy	=	7·4 per cent
Billroth I with vagotomy	=	8·0 per cent

Although mild steatorrhœa may not worry the patient, it is tempting to think it to be associated with loss of weight. Butler (1960), of Bristol, has shown that fat in stools varies with the length of the afferent loop, it being greater with the long loop and less with the short loop. The explanation would again seem to be a modification of pancreatico-cibal asynchrony in that bile and pancreatic juices are held up in the excessive loop. Two cases described later in this paper, and first published by me in 1955, are striking examples of the extreme form of this effect, though of a somewhat different mechanical origin.

During the last 45 years Dr. J. M. French has helped us considerably in advice concerning the treatment of the few cases of post-gastrectomy steatorrhœa we have had referred to us, and points out that lipase is sensitive to extremes of *p*H (Archibald, 1946; Schønheyder and Volqvartz, 1944), and that the high excretion of fat may be related to this. Thus, the Ellison–Zollinger (Zollinger and Ellison, 1955) non-beta-cell tumour of the pancreas may herald itself by steatorrhœa, our own case being a 15-st. man who, with the development of diarrhœa 3 years previously, lost weight continuously amounting to 3 st., and only developed dyspepsia during the 18 months prior to admission (Rawson, England, Gillam, French, and Stammers, 1960). His nocturnal gastric secretion amounted to 2½ litres with a *p*H of 1·0. On the contrary, the occasional case of steatorrhœa following partial gastrectomy-plus-vagotomy has achlorhydria. Is it that lipase is inactivated by these extremes of *p*H? Dr. French has suggested that we should try giving pancreatin, 2 g. in milk, during meals; antibiotics in order to modify the bacterial content (Goldstein, Wirts, and Kramer, 1961); and, latterly, we have added HCl dil.: and some improvement resulted, but not cure. In two severe cases of steatorrhœa I have converted the Billroth II gastrectomy into a Billroth I, enlarging the reservoir with a Henley loop, and adding vagotomy where it had not been previously carried out: both these patients were greatly improved.

Two other cases were of special interest, since they presented as osteoporosis, in one case with aching back and general disability, in the other with spontaneous fractures of ribs and neck of femur.

Again, they were converted into Billroth I gastrectomies using a Henley loop to increase the reservoir, and vagotomy. Both benefited so far as the steatorrhœa was concerned, and gained weight, but it is too early to speak of the calcium and phosphorus metabolic phenomena, though one is certainly building up his bones.

c. Dumping Syndrome.—By this expression is meant the patient who complains of a sensation of feeling dizzy, tired, and weary, with a strong urge to lie down, and a feeling of flushing (though they often look pale and they sweat), these symptoms coming on either shortly after taking food or three or more hours afterwards.

Many factors have been shown to be associated with this syndrome, and in some patients several may be active at the same time. The following are some of them:—

i. As long ago as 1948, Brain, whilst working with us, showed that when a balloon placed in the efferent loop of a Billroth II gastrectomy was inflated it reproduced this syndrome, even, in one or two cases, causing the patient to faint.

ii. Mix (1922) thought that food dropped from a small gastric pouch into the upper jejunum was the distending factor.

iii. Machella (1949), on the other hand, argued that it was the rapid secretion of succus entericus consequent on the sudden arrival of relatively undigested food that distended the efferent loop, whilst

iv. Le Quesne, Holsley, and Hand (1960) and others have shown that so great is this secretion and the shift of electrolytes that goes with it that there is a reduction of blood-volume—a hypovolæmia.

v. Smith (1951) studied potassium levels and found that victims of a true dumping syndrome had a passing hypokalæmia.

vi. Quite a different factor was discovered by Gilbert and Dunlop (1947), who noticed that a carbohydrate and, especially, sugar-containing meal was more likely to precipitate an attack, and suggested that it resulted from hypoglycæmia. Certainly a patient during an attack looks exactly like a diabetic on insulin who has missed a meal; or a patient undergoing the Hollander test for completeness of vagal section whereby an intravenous injection of 10 units of insulin is given and causes blood-sugar to fall to 50 or even 40 mg. per cent. They found that victims of dumping did develop this hypoglycæmia and argued that the sudden arrival of sugars in the upper jejunum stimulated the pancreas to excessive secretion of insulin. In some sufferers the syndrome comes on after about 3 hours, but in others it develops much sooner, say within 15 to 30 minutes. This should be correlated with the work of Dormandy, Leak, and Grant (1959) on the differential absorption of sugars.

vii. Finally, Butler and Capper (1951a), impressed by the rapid recovery that followed lying down, thought the phenomena to be due to the mechanical fact that the stomach was no longer slung up to the posterior abdominal wall by such structures as the left gastric artery and the gastrohepatic omentum, and that the weight of food, therefore, caused the stomach to hang on the œsophagus and diaphragm.

viii. A recent article by Cox and Allan (1960) describes radiological appearances during an actual attack that have not previously been stressed to be associated with dumping yet are well known by radiologists to be revealed during a barium meal if the patient is about to vomit—namely, a complete cessation of all peristalsis, absolute inertia. It will be interesting to study further cases. Indeed, with the image intensifier becoming more generally available, much better opportunities are offered for studying all these syndromes.

These many factors can be put under the headings distension, hypovolæmia, hypokalæmia, hypoglycæmia, mechanical, and investigation should aim at finding out which one or more factors may be operative. It can be seen that a small stomach reservoir with a Billroth II type of reconstruction could well precipitate any one of them, and to this extent enlarging the reservoir and converting to a Billroth I minimizes them. Nevertheless, the majority of patients with a Billroth II gastrectomy suffer not at all, whilst others have only minor and occasional discomfort. Simpler measures may, therefore, be sufficient, such as avoiding bulky meals or drinking during meals: or trying to sort out which particular commodity causes the trouble and cutting it out of the diet.

2. Delayed.—The discomforts referred to under this heading come on after a period—often of 3–5 years—of complete comfort, during which phase they are naturally included in the 'cured' group. The majority are of mechanical origin, though the best recognized, stomal ulcer, is due to a combination of acid secretion and the relative ischæmia of the scar tissue of the suture line. It will be dealt with first.

a. Stomal Ulcer.—The predominant symptom of stomal ulcer is pain brought on by food. It is epigastric, with a tendency to be to the left. It may come in attacks like any other peptic ulcer, and it is relieved by vomiting, though may well pass off slowly without a vomit. Hæmatemesis or melæna sometimes develops, and tests for occult blood may be positive even in the absence of the more overt type of bleeding. In the acute phase there is tenderness over the ulcer which, because of the average position of the anastomosis, is a little to the left of the midline. The ulcer following a Billroth II operation is on the jejunal side and there may be two or even more; after the Billroth I operation it is usually on the gastric side of the anastomosis. The average sufferer will think it a recurrence of the old trouble; the more intelligent will sense that though similar in many ways there are, nevertheless, differences. Barium-meal examination will often confirm the suspicion, but not always, and sometimes repeated radiographs fail to reveal the suspected ulcer. Gastroscopy will reveal those on the gastric side but may fail in those on the jejunal side. Medical means of treatment can be tried, but so often it is no more successful than for the original duodenal or gastric ulcer.

Under these circumstances, even in the event of a second negative radiograph, provided the patient is psychologically well balanced and that his home and work circumstances are satisfactory, the right thing is to advise an exploratory laparotomy. After

separating adhesions and identifying the anastomosis, the ulcer can either be seen or felt or both. Some workers suggest that vagotomy is all that is necessary but, personally, I prefer to take down the anastomosis and then to assess what further to do. If a gastrojejunostomy, I have found it best to convert to a Billroth I, using a fairly wide junction between stomach and second part of duodenum, and performing vagotomy at the same time. If the afferent loop of the original operation was of more than 10 cm. it is best to excise that part which has been detached from the stomach and to carry out an end-to-end anastomosis. The gap in the mesocolon must, of course, be eliminated by stitches. If the first operation was of a Billroth I type (and the ulcer almost certainly on the gastric side), a vagotomy alone is likely to be successful, but should the ulcer have caused a good deal of distortion or have produced considerable scarring, it is better to remove that part of the stomach affected and to re-suture; a completely new anastomosis may be indicated. Again, it is wise to add vagotomy.

Some reference should here be made of the 'inveterate ulcerater', by which is meant the patient who develops one stomal ulcer after the other in fairly quick succession, and neither vagotomy nor further excision, nor a combination of the two, proves curative; and after about three occasions one is faced with an ulcer on the cardia and the difficult question as to whether a total gastrectomy is indicated. Following the reports of Zollinger and Ellison (1955), and of Summerskill (1959), it is always worth measuring volumes and *p*H of nocturnal gastric secretions as a test for a non-beta-cell tumour or hyperplasia, though in the presence of a gastrojejunostomy this is not always easy; and when operating to look for such a tumour. I have to admit that in neither of the two inveterate ulceraters with which I have had to deal was such a tumour discovered.

b. Gastric-colic Fistula.—Fortunately rare, this is really a complication of stomal ulcer, the ones I have encountered being superimposed on the symptoms of stomal ulcer. The onset is usually relatively sudden. There may be a worsening of the pain, but the chief features are diarrhœa and fluid and electrolyte disturbance, sometimes amounting to severe dehydration and, of course, the serious malaise that goes with it. Barium-meal examination may fail to show the fistula, but a barium enema may do so. The original gastrojejunostomy is almost always of the retrocolic type and the symptoms are due to enteritis resulting from contamination by colonic contents. It is obvious that only surgical intervention will correct the situation, and until quite recent years staged procedures were considered essential. With a better understanding of fluid and electrolyte balance and how to correct imbalance, together with antibiotics, readily available blood, and better anæsthesia, it is now safe to carry out the operation at one sitting. Even so, where all laboratory and skilled assistance are not available it is still wiser to create a proximal colostomy as a preliminary preparation for reconstruction of the partial gastrectomy.

c. Loss of Weight and Energy.—This may be due to a little stomach reservoir and can be improved by increasing the number of meals per day, and giving a high-calorie diet. It may also be associated with excessive loss of fat in the stools, whether accompanied by recognizable steatorrhœa or not. Again, if present, modification of diet, together with pancreatin and antibiotics, may help. If uncontrollable, the question of conversion to Billroth I, with or without enlarging the pouch, together with vagotomy, arises.

Concerning loss of weight, it is of interest to recall Thorn, Brookes, and Whitehouse's (1956) analysis of our 955 cases with the object of finding out if there were any relationship between gastrectomy and the subsequent development of tuberculosis. They discovered that 60 of this large group developed active pulmonary tuberculosis some time after operation. All these had lost weight following operation; none who had not lost weight developed tubercle: in other words, it was a matter of poor nutrition rather than the incident of a large operation.

d. Mechanical.—

i. Due to some technical hitch at operation: In partial gastrectomy of the Billroth II type the stomach is transected at a level decided upon according to the views of the surgeon concerned. The stomach stump is held either by anchoring stitches through lesser and greater curve edges or by a clamp placed across the stomach from greater to lesser curve. In fashioning a gastrojejunostomy of the Polya type, with or without a Hofmeister valve, there is a tendency for surgeons to stick rigidly to one or other technique of 'afferent loop to lesser curve', or 'afferent loop to greater curve'. This is satisfactory so far as antecolic anastomoses are concerned, but not necessarily so in retrocolic operations. Most surgeons who have done several hundred gastrectomies have to admit to one or two cases where anxiety has been caused because within a few days of operation there seems evidence that the stoma is not fully open. Various treatments having failed to improve the situation, a small barium meal will be given which confirms that there is some degree of obstruction at the stoma. At re-operation the retrocolic anastomosis seems to have become twisted, sometimes the afferent loop lying in front, sometimes the efferent loop. When, as a routine, one makes a habit of studying the lie of the duodenojejunal junction in different patients, it is obvious that according to the arrangement of the peritoneal folds at the upper part of the mesentery, the jejunum passes from the posterior abdominal wall forward and to the left in some patients, forward and to the right in others. This arrangement should be respected when carrying out the correct 'no-loop' retrocolic anastomosis in order to avoid tension or torsion in this region. The natural lie in the former, therefore, will be effected by an afferent loop to lesser curve anastomosis and in the latter by an afferent loop to greater curve anastomosis. As Kinsella so well puts it, "there should be a quiet confluence of unobstructed streams" (Kinsella and Hennessy, 1960).

This slight twist may cause trouble in a delayed manner, symptoms suggesting gradual narrowing of the stoma coming on some years later. X-ray studies will confirm the embarrassment to the emptying of the stomach stump and re-operation is indicated.

ii. '*Obstruction-en-cocoon*': This condition occurs in retrocolic anastomosis. Two such cases come from our own series, and 6 more have been referred from elsewhere. The story is characteristic—namely, that after a period of completely satisfactory health the patient begins to suffer a little fullness after meals

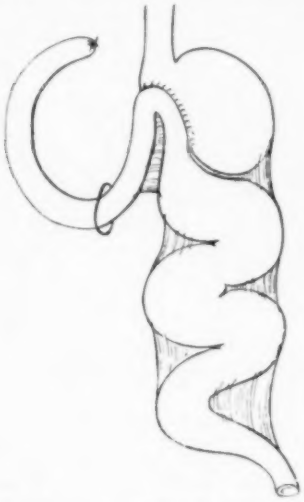

FIG. 40.—'Obstruction-en-cocoon'. (*Reproduced by permission of the Journal of the Royal College of Surgeons, Edinburgh.*)

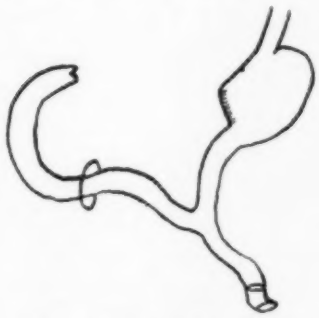

FIG. 42.—A Roux-en-Y reconstruction.

which fairly rapidly gets worse, and may be relieved by vomiting. The patient begins to modify his diet and to avoid certain things, a little later deliberately missing the odd meal. Discomfort then amounts to pain and vomiting gets worse. The patient loses weight and begins to feel and look ill, and may sense that food does not leave the stomach properly (*Fig.* 40). Two of our 8 cases said that they could actually see a fullness in the upper abdomen to the left of the midline. With observation it may be possible to confirm these features, and barium studies will show that there is some delay in passing out of the stomach.

These cases require laparotomy, and in our 7 operation cases (1 early case died whilst we were trying to solve the problem) the upper 20–25 cm. of the efferent loop was hypertrophied and enveloped in peritoneal adhesions holding it in a concertina'd, convoluted state, so that when the stomach tried to eject food into the small bowel, this loop distended, exaggerating the concertina-ing and producing partial obstruction—the best solution is to excise this

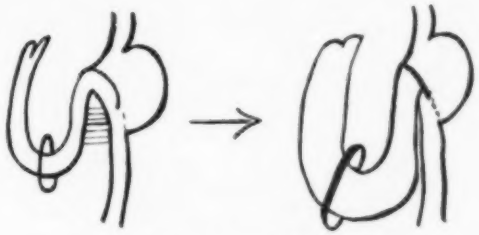

FIG. 41.—The mechanism of the afferent loop syndrome. (*Reproduced by permission of the Medical Press.*)

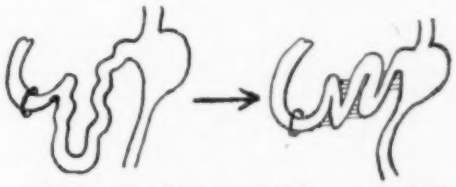

FIG. 43.—Long afferent loop having become concertina'd. (*Reproduced by permission of the Birmingham Medical Review.*)

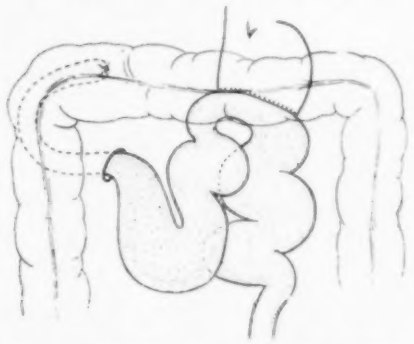

FIG. 44.—Retrocolic Polya gastrectomy: concertina'd efferent loop causing obstruction and pressure on too long afferent loop. (*Reproduced by permission of the Journal of the Royal College of Surgeons, Edinburgh.*)

thickened loop and convert to a Billroth I operation, adding vagotomy.

All the 7 cases have done well.

iii. *Afferent loop syndrome*:—

α. True afferent loop syndrome, as described by Wells and Welbourne (1951), and by Steinberg (1949). The symptoms are again characteristic, consisting of fullness or frank pain shortly after food, relieved only by vomiting, the vomit consisting of pure bile, or food heavily mixed with bile. Again, there is a long period of good health before the symptoms come on. Wells and Welbourne's explanation seems the most satisfactory, and suggests that over the course of years adhesions develop which

tether the afferent and efferent loops together and distort the anastomosis at the afferent loop end, these together forming some partial obstruction of the afferent loop. With the arrival of food in the stomach, bile and pancreatic juices are secreted into the afferent loop but cannot get out because of these distorting factors (*Fig.* 41). The tension causes pain

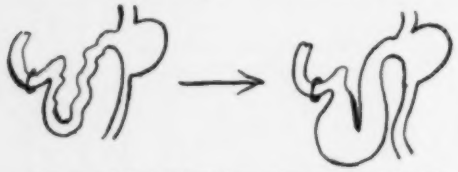

FIG. 45.—A long afferent loop acting as a sump for bile and pancreatic juices, thus delaying their proper mixture with food and consequent steatorrhœa. (*Reproduced by permission of the Annals of the Royal College of Surgeons.*)

and the obstruction can only be overcome by powerful peristalsis which eventually causes a vomit (200–400 ml.) of almost pure bile: this is most characteristic. Operation is called for. Wells and Welbourne and, later, Steinberg, suggested the pantaloon modification of entero-enterostomy, but Hall of York (1959), at meeting of Moynihan Chirurgical Club, suggests a Roux-en-Y reconstruction. Our 2 cases have done very well following this latter operation (*Fig.* 42).

β. Convoluted long afferent loop: I have pointed out elsewhere (1952) the disadvantage of using an afferent loop of more than about 10–15 cm. One of these is that such may become wrapped up in peritoneal adhesions, causing a concertina-ing and thereby a steadily increasing embarrassment to the passage of secretions along the loop (*Fig.* 43). From a symptomatic point of view it mimics the simpler afferent loop syndrome, and demands excision of the excessive loop and a Roux-en-Y reconstruction. We have had 6 such cases, 2 being from our own series, and the results have been most gratifying. Five were antecolic operations, but 1 was retrocolic and possibly because of its crowded position to the left of the vertebral column it had become enclosed in a translucent bag of peritoneal adhesions (*Fig.* 44). The efferent loop also had undergone a similar change and some element of obstruction was produced.

iv. '*Sumping*': Yet another, though rare, delayed complication of an over-long afferent loop was

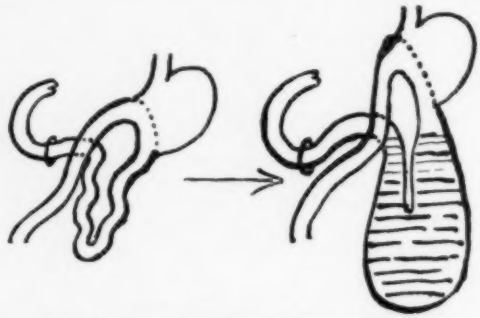

FIG. 46.—Long afferent loop to greater curve becoming dilated and acting as a sump containing bile and pancreatic secretions.

recorded in 1955 (*Fig.* 45). Two cases have been referred to the Teaching Hospital in Birmingham; one to Dr. C. Hawkins and one to myself. Both patients had had a partial gastrectomy operation of the Billroth II type for peptic ulcer, and both had enjoyed several years of good health. Then in each patient diarrhœa began to develop followed by malaise, loss of weight, and discomfort, and the diarrhœa was found to be due to steatorrhœa. Laparotomy was decided upon and in each case the long afferent loop was found to have become dilated and the wall thickened and capable of holding up to 200–300 ml. of secretions. In the first case the anastomosis had been afferent loop to lesser curve (*Fig.* 45); in the second, afferent to greater curve

FIG. 47.—Radiograph showing gross dilatation.

(*Fig.* 46). The cause of the dilatation was not apparent, but the effect was to retain the bile and pancreatic juices too long for proper admixture with the stomach contents passing into the efferent loop—another form of pancreatico-cibal asynchrony, and reminiscent of the observations, already mentioned, being carried out in Bristol. Radiographs were suggestive of this gross dilatation, and operation consisted of removing the excessive and sump-like afferent loop followed by reconstruction (*Fig.* 47).

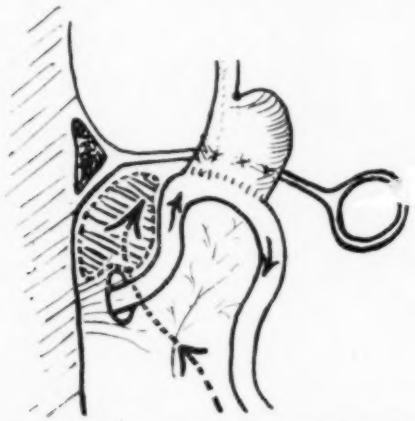

FIG. 48.—The case of retrocolic gastrectomy in which efferent loop passed from right to left through the gap, as described by Peterson (1900).

In patients developing steatorrhœa some years after a Billroth II type gastrectomy, and in the absence of the more usual causes, it is well to remember this sumping possibility. Our second case was rescued from a mental hospital by a psychiatrist who had heard discussions on the delayed complications of gastrectomy.

v. *Loop-the-loop syndromes*: First recorded by Peterson in 1900 and re-described by Stammers in 1952, to which have been added papers of all published cases in the past 60 years, these herniations may take place during post-operative convalescence or as a delayed event, even occurring several years after the original operation, and more and more of these delayed cases are being reported. A typical history is that the patient has progressed well following the operation, and has continued in good health until there is a fairly sudden onset of upper central abdominal pain accompanied by nausea and, later on, vomiting. The pain is at first mild and intermittent, but as vomiting becomes more frequent the pulse rises and, depending on duration, dehydration may become obvious. On examination there is no distension or rigidity, though there may be an indefinite mass to the left of the midline. The picture is one of a partial, high intestinal obstruction. Intravenous therapy and suction bring about great improvement, but as soon as the Ryle's tube is removed symptoms return. Laparotomy is called for, and, keeping in mind the six or seven varieties of these herniations (Stammers, 1954), it is usually possible to reduce them. Needless to say, the gap through which the loop of gut has passed should be closed by stitches—it should, of course, have been closed at the time of the original operation, as I pointed out in 1952. Sufficient has been said in the past describing the varieties, but for convenience sake *Figs.* 48–50 portray some of them.

It may justifiably be argued that with modern techniques—namely, removal of not more than about three-fifths or less of the stomach, plus vagotomy—called now in the United States 'antrectomy and vagotomy'—many of these post-gastrectomy complaints should be avoided. Yet there are large numbers of patients from whom seven-eighths or even nine-tenths of their stomach has been removed in days gone by who need help because of one or other pattern of these discomforts; and still more are being

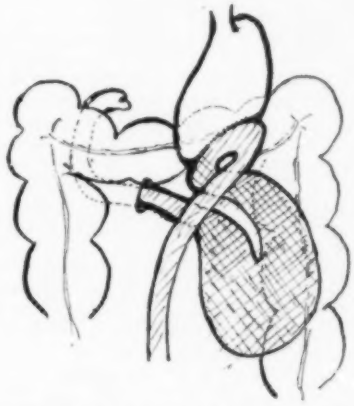

FIG. 49.—Long afferent loop passing from right to left through the gap. (*Reproduced by permission of the Annals of the Royal College of Surgeons.*)

FIG. 50.—In this case, a loop of ileum passed from left to right through the gap (efferent loop to lesser curve).

produced in some areas by a continued employment of these older-fashioned major gastrectomies. If approached, as suggested, one can quite often analyse the cause, and thereby offer rational treatment.

In summary, and based on symptom-patterns, it comes to this:—

1. *Immediate.*—

a. Early fullness, inability to eat full meals, and loss of weight and energy—little stomach.

b. Loose stools, feeling of food hurrying through the bowel, inability to gain weight—may be a little-stomach factor again; or unsuspected steatorrhœa, probably in excess of the levels of Gobbel, Shoulders, and Main (1960).

c. True steatorrhœa with all the malaise, loss of weight, and energy that this causes. Here one must exclude cœliac disease, pancreatic disease, and the malabsorption syndromes, and consider the possibility of the effects of extremes of *p*H on gastric and pancreatic lipase. Simple measures may help, but conversion to Billroth I, together with enlarging the reservoir and vagotomy, certainly helps.

d. The true dumping syndrome, assessing the factors of distension, hypovolæmia, hypokalæmia, hypoglycæmia, and mechanical. Here, again, simple dietetic measures may help, but conversion to Billroth I, with or without enlarging the reservoir, plus vagotomy, is worthy of consideration if incapacitating.

2. *Delayed.*—

a. Loss of weight and energy—little stomach; or subclinical steatorrhœa.

b. Pulmonary tubercle—associated with underweight.

c. Anæmia—of high incidence following gastrectomy.

d. Stomal ulcer. Gastrocolic fistula.

e. Symptoms suggesting interference with free outlet through stoma and upper few inches of efferent loop—twist or torsion of gastrojejunostomy; or 'obstruction-en-cocoon' of efferent loop.

f. Fullness and pain during or after meals relieved by a vomit of almost pure bile—afferent loop syndrome, either simple or due to a concertina'd long afferent loop.

g. Delayed onset of steatorrhœa—as for the early type, but also the possibility of 'sumping' of a too-long afferent loop.

h. Fairly sudden onset of high intestinal obstruction, relieved by suction, but recurrent on removal of suction—one of the patterns of herniation through the man-made gaps produced by the anastomosis.

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CONGENITAL ABNORMALITIES OF THE ANUS AND RECTUM

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CONGENITAL abnormalities of the anus and rectum occur approximately once in every 5000 births (Bradham, 1958). They may be divided into two main groups, the high and the low, depending on whether the termination of the bowel is above or below the pelvic floor. This is the most important single factor with regard to treatment and prognosis. The low abnormalities are usually easy to diagnose, simple to treat, and have a favourable prognosis; the high abnormalities are frequently associated with a fistulous communication with the lower urinary tract or vagina and this, together with poor development of the pelvic floor, combines to make treatment more difficult and its results less satisfactory.

The classification adopted here is based on the study of a series of 323 cases of anorectal abnormalities seen at the Hospital for Sick Children, Great Ormond Street, in the 10-year period January, 1949, to December, 1958. These children have been under the care of one of seven surgeons during this period, some having had their initial treatment elsewhere. Variations in the method of treatment of any one condition, therefore, occur in the series. The opinions expressed are our own and are based on these cases; we hope the descriptive nature of the classification will help to resolve the confusion which has arisen owing to the multiplicity of names by which some of these conditions are known.

The common high anomalies are caused by some early defect in organization of the pelvic viscera of the embryo. The low anomalies result from one of two later faults in development, either failure of migration of the terminal bowel which results in the ectopic anus, of which the vulval and perineal types are the most common, or excessive fusion of fœtal tissues resulting in the stenosed anus or the covered anus.

CLASSIFICATION

Low Abnormalities:—

1. The covered anus.
2. The ectopic anus.
3. The stenosed anus.
4. Anal membrane.

High Abnormalities:—

1. Anorectal agenesis, with or without fistula.
2. Rectal atresia.
3. Cloaca.
4. Multiple abnormalities.

The term 'imperforate anus', although well recognized, has been avoided, because in the past it has been used to describe more than one condition, and also because it is felt that its use either as a specific or comprehensive description has delayed recognition of the important distinction between the high and the low anomalies.

The terms 'agenesis' and 'atresia' are used in accordance with their meanings (*Shorter Oxford Dictionary*) of imperfect development and occlusion, respectively. They have sometimes been used synonymously in the description of anorectal abnormalities, but here 'rectal atresia' is used to describe the condition in which there is segmental occlusion (as, for example, in duodenal atresia) and 'anorectal agenesis' describes imperfect development (as, for example, in renal agenesis).

The term 'cloaca' is used to describe the severe abnormality in which the urinary, genital, and alimentary tracts all open into a common cavity.

CLINICAL DESCRIPTION OF ABNORMALITIES

Low Anomalies (syn. anal anomalies).—

The Covered Anus (syn. Ladd Type 3 with rectoperineal fistula) (*Fig.* 51).—In this anomaly, which might be called 'covered anal canal' and which occurs much more commonly in the male, the anus is absent, but the presence of an underlying anal canal is denoted either by a bar of skin, usually A-shaped, or by a narrow midline track filled with green or white meconium running forwards on the perineal raphe. The track may extend along the perineum as far as the scrotum, or rarely may pass superficial or deep to the scrotum to appear on the ventral aspect of the penis. In a rare variant of the low anomaly described by Young (1936) there is a low opening of the bowel into the membranous urethra and an associated hypospadias.

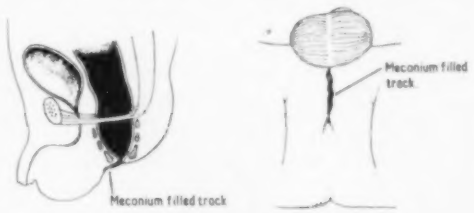

FIG. 51.—Covered anus.

Diagnosis is straightforward when a track is present or a A-shaped bar of thickened skin overlies the anal canal; Nixon (1959b) considers that one or other of these is always present. In our experience, however, there may sometimes be difficulty in differentiating the bulging of the whole perineum during crying in cases of the high termination, and if doubt exists the X-ray technique described by Wangensteen and Rice (1930) or that of Stephens (1953a) is indicated. In the former a small piece of lead shot is applied with sticking plaster to the supposed site of the anus and the infant held upside down for 3–4 minutes. Air displaces meconium from the distal distended bowel and a lateral film is taken. If the distance between the air bubble and the lead shot is

* Now at North Devon Infirmary.

† Now at Peter Bent Brigham Hospital, Boston, Mass., U.S.A.

over 1 in. (2·5 cm.) the termination is high; an antero-posterior radiograph is liable to give an erroneous impression of this distance owing to tilting of the pelvis.

Stephens describes the pubococcygeal line as joining the upper border of the symphysis pubis to the sacrococcygeal junction. When a lateral radiograph centred over the great trochanter, with the child inverted, is taken, the gas bubble in cases of

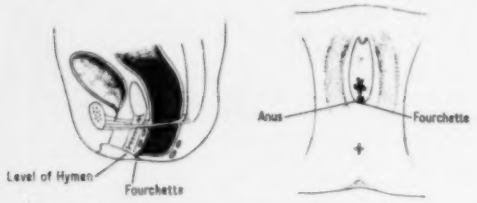

FIG. 52.—Vulval ectopic anus.

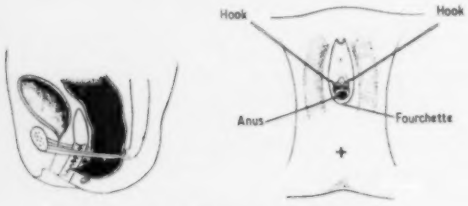

FIG. 54.—Vaginal ectopic anus.

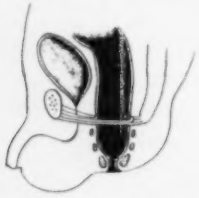

FIG. 56.—Anal membrane.

anorectal agenesis in the male will ascend only to this level. In the covered anus the bubble will ascend farther to the level of the lower border of the ossified ischial bone.

False results may be obtained in both methods. The meconium may be so tenacious that it is not displaced by the air in the distended distal bowel, or there may be insufficient gas in the first 24–36 hours of life to act as a contrast medium.

The Ectopic Anus.—The anus is situated anteriorly to its normal position. The mildest degree of abnormality and the form which is found in the rare male cases is the *perineal ectopic anus*. If the opening is within the limits of the labia majora, the abnormality is known as '*vulval ectopic anus*' (*Fig.* 52). There is usually stenosis of the external orifice in both these varieties, which have as their synonyms in other methods of classification 'Ladd Type 3 with rectoperineal fistula' and, in the case of the vulval ectopic, the 'shotgun perineum of Denis Browne'. In the *vestibular ectopic anus* (*Fig.* 53) the bowel opens into the vestibular fossa, which is a depression bounded superiorly by the hymen and inferiorly by the fusion of the labia minora, viz., the fourchette or frenulum. Its relation to the hymen differentiates it from the least common variety, the *vaginal ectopic anus* (*Fig.* 54) which opens above this membrane yet below the pelvic floor (Ladd Type 3 with recto-vaginal fistula).

In all four varieties continence may be established because of the normal levator ani muscle. Evidence

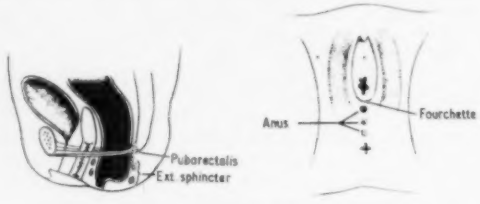

FIG. 53.—Vestibular ectopic anus.

FIG. 55.—Anal stenosis.

of the external sphincter apparatus is found in the perineal and vulval types; its development in the vestibular and vaginal types is variable but usually is deficient to a greater or lesser degree.

The Stenosed Anus.—This anomaly (syn. Ladd Type 1) occurs more frequently in males than females. The anus is in its normal position but may be so small that it is almost invisible (the microscopic anus of Denis Browne) and the baby may appear to have a covered anus or anorectal agenesis (*Fig.* 55). Careful examination will, however, reveal a minute opening, perhaps covered by a speck of meconium. Alternatively, the anus may be easily visible but, together with the anal canal, be smaller in calibre than normal. A form of membranous stenosis is discussed in the next section.

Anal Membrane (syn. Ladd Type 2) (*Fig.* 56).—The anus is normally situated but the canal is obstructed at the level of the anal valves by a membrane which, when the infant strains, may be seen bulging with retained meconium. In contrast to popular opinion, this anomaly is extremely rare. It has been confused in the past with a covered anus, where the covering is very thin, and also with Hirschsprung's disease when withdrawal of the examining finger is often followed by a gush of meconium. Should the membrane partially rupture, a membranous stenosis will result.

High Anomalies (syn. rectal anomalies).—

Anorectal Agenesis (syn. Ladd Type 3, imperforate rectum, rectal agenesis) (*Fig.* 57).—This anomaly occurs considerably more frequently in males than females. The anus, anal canal, and lower

rectum are absent and the blind rectal pouch, lying just above the pelvic floor, becomes distended with meconium and air and enlarges to fill the pelvis. From its anterior aspect in the male it is attached to the urinary tract. In a few instances this attachment is by a fibrous cord, but in the majority there is a fistula communicating with the proximal urethra, cavity. As is explained in the section on embryology, this anomaly occurs only in females. There is ano-rectal agenesis, a high opening of the urethra or bladder directly into the common cavity, and usually duplication of the uterus. Mucocolpos presenting as an abdominal tumour is not uncommon. The external opening of the cloacal cavity may be of the

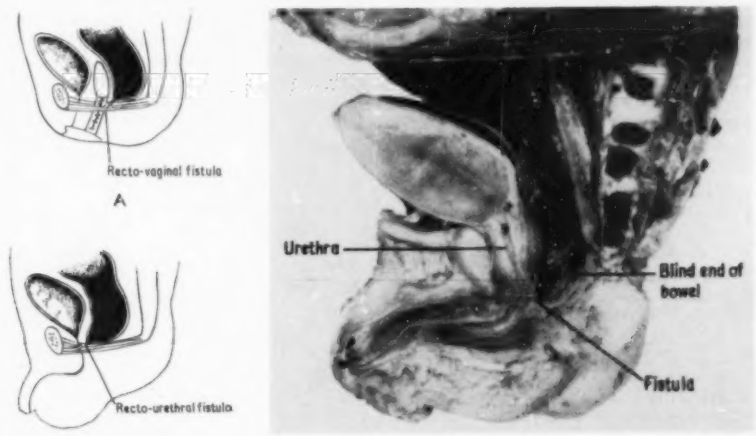

FIG. 57, A, B, Anorectal agenesis; C, Anorectal agenesis with recto-urethral fistula. (The opening of the fistula into the urethra is lower than is usual.)

which manifests itself clinically by the passage of meconium or gas in the urine. Rarely the fistula may enter the bladder. In the female the abnormality is essentially the same, except that the interposed Müllerian system separates the alimentary from the urinary tract and the blind rectal pouch is attached to the posterior vaginal fornix. This attachment is usually patent in the form of a fistula but, as in the male, may be only a fibrous cord. Anomalies of the Müllerian system, usually caused by incomplete fusion, frequently coexist so that the relationship of the terminal bowel to the uterus and vagina may be variable.

The external sphincter is represented by mal-developed muscle-fibres, although there may be a suggestion of a dimple in the perineum. The levator ani (when seen at operation) may be lacking in one or more of its constituent parts, e.g., ileococcygeus; the degree of differentiation of the pelvic floor and the innervation of the pelvic viscera seem to be commensurate with the development of the sacrum. Williams and Nixon (1957) found that there were no cases of urinary continence in otherwise normal children when sacral development was limited to three segments.

Rectal Atresia (syn. Ladd Type 4) (*Fig.* 58).—The bowel ends blindly above the pelvic floor without a fistulous opening into the urinary tract. The anal orifice is normal and the anal canal, which is surrounded by a normal external sphincter, ends blindly at the level of the pelvic floor. The anomaly is uncommon and is the same in both sexes.

Cloaca.—In these infants the bowel and the urinary and genital tracts open into a common wide normal size of the vaginal introitus, or it may be very small and be mistaken for an external urinary meatus. Other severe abnormalities often coexist.

Multiple Anomalies of which Anorectal Agenesis forms a Part.—A severe malformation also exists in which most of the colon, rectum, anal canal, and

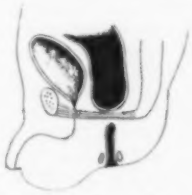

FIG. 58.—Rectal atresia.

anus are absent. This combination of abnormalities, known as 'ectopia cloacæ' (Williams, 1958), consists of agenesis of the hindgut, exomphalos, ectopia vesicæ, and vesico-intestinal fissure, whereby ileum prolapses through a patent omphalomesenteric duct, together with split scrotal elements in the male and diphallus. There is often associated severe malformation of the heart and great vessels.

EMBRYOLOGY

The cloaca is formed by the development of the tail fold, its lining epithelium is endodermal, and its cavity receives the hindgut, the allantois, and the developing mesonephric ducts. The cloacal membrane forms one of its boundaries and from the ectodermal aspect of the embryo is seen to lie in a

depression, sometimes called the 'ectodermal cloaca', which is bounded on either side by the genital swellings and genital folds.

During the fourth and fifth weeks, when the embryo is about 5 mm. crown-rump length, the hind end becomes the site of very active growth. As the tail fold develops, the cloaca becomes divided by the growth of the urorectal septum in the angle between the allantois and the hindgut (*Fig.* 59). It is likely also that the separation of the hindgut from the 'urogenital sinus', as the remaining part of the cloaca is now called, is partly effected by differential growth associated with the tail-fold formation. As the urorectal septum descends the communication between these two cavities becomes progressively smaller, finally being known as the 'cloacal duct'. With the fusion of the septum and the cloacal membrane, this duct becomes obliterated and the membrane becomes divided into its urogenital and anal parts, which soon after break down to allow the ectodermal and true cloacæ to communicate. In the male the genital folds bordering the urogenital sinus fuse to form the bulbous and penile urethra (pars spongiosa). In the female they remain unfused to form the labia minora; they do, however, meet anteriorly at the clitoris and posteriorly at the fourchette. The female urethra and the vestibule are derived from the caudal part of the urogenital sinus.

Posteriorly the ectodermal cloaca is separated from the tail fold by two anal tubercles which are fused in the midline (*Fig.* 60). With the descent of the urorectal septum, these two tubercles fuse anteriorly, both with each other and the septum itself, thereby forming the proctodeum. Mesoderm which invades this area forms the external sphincter, the perineal musculature, and the perineal body. As the latter develops, the anus undergoes a 'posterior migration' to reach its definitive position. The site of the anal membrane is generally accepted as being at the level of the valves at the lower limit of the anal columns. The part of the anal canal above this limit is derived, therefore, from the hindgut and the part below from the proctodeum.

The remaining general aspect of embryology relevant to the discussion of the abnormalities of this region is the development of the Müllerian system. The Müllerian ducts, which are formed from cœlomic epithelium lateral to the mesonephric ducts, meet in the midline between the hindgut and the urogenital sinus and fuse with each other to form the uterovaginal canal. The caudal tip of this canal joins the posterior wall of the urogenital sinus to form the Müllerian tubercle, and the endodermal cells lining the sinus at this site proliferate to form the sinuvaginal bulbs (*Fig.* 61). From these bulbs and the solid cord of cells—the uterovaginal cord—which develops from the lower end of the uterovaginal canal the vagina is formed (Koff, 1933) Some authorities, however, consider that the whole of the vagina is formed from the uterovaginal cord. The uterus and Fallopian tubes are derived from the more proximal uterovaginal canal.

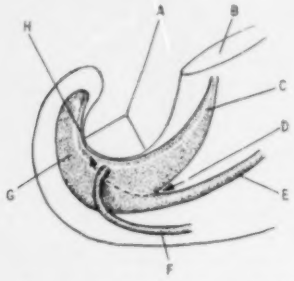

FIG. 59.—A, Cloacal membrane; B, Body stalk; C, Allantois; D, Urorectal septum; E, Hindgut; F, Mesonephric duct; G, Cloacal cavity; H, Tail gut.

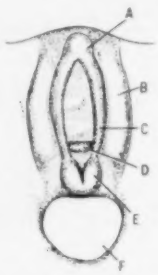

FIG. 60.—A, Genital tubercle; B, Genital swelling; C, Genital folds; D, Urorectal septum (seen through cloacal membrane); E, Anal tubercles; F, Divided tail fold.

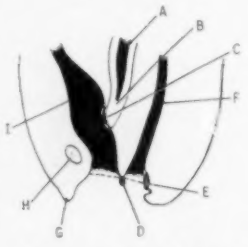

FIG. 61.—A, Uterovaginal canal; B, Uterovaginal cord; C, Sinuvaginal bulb; D, Urorectal septum; E, Anal tubercle and level of anal membrane; F, Hindgut; G, Genital tubercle; H, Symphisis pubis; I, Urogenital sinus.

The Covered Anus.—Following a theory first suggested by Wood Jones (1915), Denis Browne (1950) and Stephens (1953a, b) have offered an explanation of the common low abnormality found in the male, known now as the 'covered anus'. The ectodermal cloaca is bounded laterally by the genital swellings, destined to form the labia majora or scrotum, and by the inner genital folds, whose fate has already been described. Posteriorly the genital folds are continuous with the anal tubercles (Tench, 1936), and if in the male the fusion of these folds should extend too far posteriorly, the anus itself will be covered. Occasionally the covering skin may break down on either side of the resulting thickened midline raphe to expose an anus divided by a median bar.

This overfusion occurs much less frequently in the female; when it does, the 'covered vagina' results. If the fusion is extreme external examination will show a perineum with a small opening at the base of the clitoris and in such cases the differential diagnosis must be made from pseudohermaphroditism.

The narrowing of the anus and anal canal in *anal stenosis* is caused by excessive fusion of the anal tubercles during the formation of the proctodeum; this fusion is also often accompanied by a shortening of the canal. If the anal membrane fails to break down, a rare occurrence, the condition known as '*anal membrane*' results.

Anorectal Agenesis.—It must be very unusual for infants to have a normally developed proctodeum in association with anorectal agenesis and fistula, although Keith (1908) reported 7 out of 10 females and 4 out of 7 males with a normal proctodeum and in his text-book on embryology (1949) he represents these cases diagrammatically; we have seen no such cases. Several theories have been advanced to attempt to explain the anomaly. Wood-Jones (1904) postulated that the portion of the rectum which develops from the hindgut extends from Houston's first fold to the third fold, this latter corresponding in level to the peritoneal reflection. He considered that this part represented the rectum in cases of anorectal agenesis and called it 'the pelvic part of the rectum'. Below the level of Houston's third fold he suggested that the 'perineal part of the rectum' developed from a post-allantoic outgrowth of the cloaca which extended to the level of the anal valves, this perineal part being absent in infants with anorectal agenesis. This theory accounted for the type of abnormality described at the time and might explain normal proctodeal development in the presence of the high abnormality; this, however, is a rare occurrence. Also it might be reasonable to suggest that, if the post-allantoic theory were true, one might occasionally find a recto-urethral or rectovesical fistula without anorectal agenesis. This is not recorded.

Keith felt that Wood-Jones's theory was untenable and based his reasoning on comparative studies. He considered that the descent of the urorectal septum could be represented as a migration of the opening of the hindgut into the cloaca—i.e., the primitive anus—due to the differential growth of a mass of plastic mesodermal tissue in which the hindgut was ensheathed. Arrest of this migration at any stage would lead to the persistence of a connexion between the hindgut and the genito-urinary system. In the male this fistula would connect with bladder or urethra. In the female the Müllerian system, as it were, 'takes up' the fistula as the uterovaginal cord grows caudally and the opening is, therefore, between gut and vagina. This theory has recently been supported by Bill and Johnston (1958).

The constancy with which the recto-urethral fistula enters the prostatic urethra suggests to us that it is possible that in these high abnormalities the urorectal septum does not descend at all, or, in Keith's theory, that the plastic mesoderm which represents the septum does not produce a migration of the anus. Possibly it is the complex changes which occur in the wall of the urogenital sinus, producing the separation of the mesonephric and metanephric (ureteric) ducts and the reversal of their relative positions, which cause the orifice of the hindgut to open almost constantly into the part (pars pelvina) of the urogenital sinus which later forms the prostatic urethra.

In the female a *vestibular ectopic anus* will be produced if the termination of the hindgut is carried down before the sinuvaginal bulbs. If, however, the hindgut becomes incorporated in the sinuvaginal bulbs, or uterovaginal cord proximal to the bulbs, the fistula may occur at any level in the vagina—the *vaginal ectopic anus*. or *anorectal agenesis* with rectovaginal fistula. Should the termination of the hindgut be carried down normally and then the perineum fail to develop fully, the anus will remain anterior to its normal position—the *vulval* or *perineal ectopic anus*.

Cloaca.—In the female anorectal agenesis may occasionally be associated with a high opening of the urinary tract into the 'vagina'; such infants may be said to have a '*cloaca*' (Gough, 1959). This term does not postulate the complete persistence of the embryological cloaca, only a part of it, into which open the urinary, genital, and alimentary tracts. Usually these children have other severe abnormalities in the genito-urinary tract, such as agenesis of the urethra, megacystis, bifid uterus, septate vagina, or mucocolpos, and also of the other systems, one or all of which may prove incompatible with life. A cloaca in a male infant has not been seen by us. The genital or mesonephric ducts (the vasa) do open into the prostatic urethra with the rectal fistula, but there is no dilated cavity. From the clinical point of view, therefore, we have regarded these cases as anorectal agenesis with recto-urethral fistula, although Nixon (1959a) classifies them as cloacæ.

Rectal Atresia.—It is difficult to explain this unusual anomaly by Keith's theory; however, it is tempting to suggest that its cause is the same as that of ileal atresia. Recent experimental work by Louw (1959) has demonstrated that ileal atresia in puppies *in utero* can be produced by obstructing the arterial supply to part of the gut. Animals so treated are born with classical atresia of the small bowel. Such vascular interference in the human fœtus may follow antenatal volvulus, but often its cause is unknown. It would seem, however, that the factor which affects a branch of the superior mesenteric artery to a segment of the ileum might also affect the superior rectal branch of the inferior mesenteric artery, producing rectal atresia. This theory is supported by an operative finding in one of our cases of rectal atresia. From the proximal blind loop of bowel a cord of what appeared to be fibrous tissue was seen passing back towards the sacrum. This was excised and on section proved to be a segment of atretic bowel. Such 'fibrous' cords are commonly found between the proximal and distal bowel in ileal atresia, and have also been described in this position in rectal atresia (Stephens, 1953b).

The cause of anorectal, as of most other anomalies, remains unknown. That a genetic factor may be involved is suggested by the finding of three families in this series with more than one similarly affected member.

INCIDENCE

The incidence of the various abnormalities set against the table of classification is recorded in *Table I*. The percentages expressed represent the numbers of each anomaly compared with the total of all anomalies. It will be seen that the low anomalies account for 60 per cent and the high 40 per cent of the total. The sex incidence of low and high anomalies together was: males, 57·3 per cent (185 cases); females, 42·7 per cent (138 cases).

Of the low anomalies which occur in both sexes there was a strong male preponderance, only 9 of the 38 cases of anal stenosis occurred in females and only 5 of the 53 cases of covered anus. Cases with a stenosed anteriorly placed anus accompanying

ectopia vesicæ (extrophy of the bladder) have been excluded from the series.

The great majority of high anomalies occur in males, which has been explained already as due to the influence of the development of the Müllerian system between the alimentary and urinary systems. Almost 33 per cent of the total anomalies were male high abnormalities compared with only 7 per cent female.

Table I.—Incidence of Congenital Abnormalities of Anus and Rectum

	Cases	*Per cent*
Low Abnormalities:—		
Covered anus	53*	16·4
Ectopic anus:		
Perineal, Vulval	57	17·6
Vestibular	33	10·2
Vaginal	8	2·5
Stenosed anus	38	11·8
Anal membrane	3	0·9
	192	59·4
High Abnormalities:—		
Anorectal agenesis:		
Male	103	31·9
Female	11	3·4
Rectal atresia	5	1·6
Cloaca	9	2·8
Multiple anomalies:		
Ectopia cloacæ	3	0·9
	131	40·6

* Included here is the one case of hypospadias and anobulbar fistula (*see* p. 37).

Table II.—Associated Anomalies in Cases with Low Abnormalities

Vertebral:—	
Sacral malformations	16
Lumbar hemivertebræ	3
Spina bifida	4
Congenital scoliosis	1
Other Skeletal:—	
Talipes equinovarus	1
calcaneovalgus	2
Congenital dislocation of hip	1
Deformity of thumb	2
Syndactyly of toes	1
Cardiovascular:—	
Congenital heart disease	7
Coarctation of aorta	1
Hæmangiomata	3
Urinary:—	
Absent or non-functioning kidney	5
Hydronephrosis or hydro-ureter	2
Ectopic kidney	1
Genital:—	
Hypospadias	4
Corkscrew penis	1
Bifid scrotum	2
Septate vagina	3
Alimentary:—	
Œsophageal atresia	2
Meckel's diverticulum	1
Malrotation	1
Atresia of bile-ducts	1
Nervous system:—	
Mental retardation	2
Cerebral agenesis	1
Others:—	
Cleft palate	3
Cretinism	1
Sacrococcygeal teratoma	1
Umbilical hernia	1

Age of Referral to the Hospital for Sick Children.—In those cases of low anomaly in which early treatment was required for intestinal obstruction, e.g., covered anus, referral was within the first week of life. Where the passage of a milk stool was not noticeably impeded, as in the vulval ectopic anus or in some cases of anal stenosis, the deformity frequently remained unnoticed in the first two weeks of life.

Seventy-six of the 114 cases of anorectal agenesis were referred in the neonatal period, and of the remaining 38 which had initially been treated elsewhere two-thirds (23 cases) were referred between the ages of 1 and 5 years. In most instances the decision to refer the child was taken following the appearance of urine from the blind loop of the colostomy (one child was 4¾ years old before this occurred), or because of the prospect of attending school with a permanent colostomy.

ASSOCIATED ABNORMALITIES

Many of these infants, especially those with high abnormalities, have associated congenital abnormalities. This is not surprising, for the pelvic viscera are differentiating from the cloacal cavity at about the 6-mm. stage, i.e., 5 to 6 weeks, and at this stage other systems, notably the upper alimentary and cardiovascular, are also undergoing important changes. They too are susceptible to the factor which interferes with organization in the rapidly differentiating embryo.

There were 114 cases of anorectal agenesis and 71 (62·3 per cent) of these had other, often multiple, abnormalities. All the cases of cloaca and ectopia cloacæ were so affected, but only 1 of the 5 cases of rectal atresia. Of the 192 cases of low anomaly, 48 (25 per cent) had associated abnormalities. Other abnormalities were discovered by clinical examination, by inspection of available radiographs, and by

Table III.—Associated Anomalies in Anorectal Agenesis

Vertebral:—	
Sacral—abnormal fusion	4
partial or total agenesis	9
Lumbar—abnormal number	3
hemivertebra	3
Dorsal—hemivertebra	1
Spina bifida	6
Other Skeletal:—	
Congenital dislocation of hip	2
Talipes equinovarus	1
Deformity of thumb or fingers	2
Torticollis	1
Agenesis of abdominal muscles	1
Congenital Heart Disease:—	
Ventricular septal defect or Fallot's tetralogy	11
Dextrocardia	1
Patent ductus arteriosus	1
Urinary:—	
Absent or non-functioning kidney	14
Hydronephrosis	10
Epispadias or ectopia vesicæ	1
Diverticulum of bladder	1
Horseshoe kidney	4
Polycystic kidney	1
Duplex kidney	1
Mega-ureter	1
Genital:—	
Hypospadias	1
Incomplete or absent genitals	2
Bifid scrotum	1
Hydrocolpos	1
Bifid uterus or septate vagina	2
Gastro-intestinal:—	
Œsophageal atresia	14
Duodenal atresia	1
Diaphragmatic hernia	2
Agenesis of bile-ducts	1
Nervous System:—	
Mongolism	3
Microcephaly	1
Cleft Palate	1

operative and autopsy findings. A list of abnormalities associated with the low and high anomalies is given in *Tables II* and *III*. Of 103 instances of anorectal agenesis in the male, 78 had an established recto-urethral fistula, and the presence of a fistula was suspected in a further 9 cases. This high incidence has led us to regard recto-urethral fistula as a feature of the anomaly, rather than an associated abnormality.

The frequency with which urinary and anorectal anomalies are associated has been appreciated only in the last few years; it is now considered advisable in all these children to perform an excretory pyelogram. In the absence of urinary infection this may be postponed until the infant is 1 year old (here it is pertinent to quote Williams's (1958) statement that a *proteus* or *pyocyaneus* urinary infection in infancy usually signifies the presence of a congenital anomaly of the urinary tract). The year's delay will ensure more satisfactory radiographs and will also diminish the radiation risk; this point may be important if an anomaly is found as treatment and follow-up will involve repeated X-ray examinations. Of the 131 cases of high anomaly in this series, pyelograms have been traced for 28; 15 of these showed an abnormality, ranging from absence of one kidney to uni- or bilateral hydronephrosis. In the low anomalies in the female, of which there were 111 cases, 11 cases were found to have had pyelograms and 4 of these showed an abnormality. Of the 81 cases of low anomaly in the male, only 1 case had had a pyelogram and this revealed a non-functioning left kidney. It is not suggested that these figures give any true indication of the frequency of urinary abnormalities as so few cases have been subjected to pyelography and a degree of selection has probably occurred; they do, however, stress the need for this investigation.

TREATMENT AND ITS RESULTS

Treatment aims at providing an anus of normal calibre at the normal site, over which the child has full control. Treatment of low anomalies may be expected to be relatively brief and in the great majority of children (86 per cent) is followed by good results, whereas in the high anomalies it is prolonged, often attended by complications involving the urinary system, and, even after a long period of post-operative supervision, its outcome may vary from a state approaching normality to one equivalent to a perineal colostomy. Complete obstruction must be relieved early, but in these infants the fear of strangulation need not precipitate operation; time may be taken, for example, to transfer the baby to another hospital.

After studying the cases in this series certain general points became evident:—

1. When there is one congenital anomaly, another may coexist. It should be unnecessary to stress the need for a full and careful examination of the baby, but only by continual repetition of this discipline will associated anomalies be discovered.

2. The newborn baby withstands major surgery well. In addition to the management of the different fluid requirements in the newborn period, care is needed to ensure maintenance of a constant body temperature during and after operation.

3. Post-operatively the maintenance of a clear airway is of paramount importance. The newborn baby resembles the unconscious adult in that stomach contents may be silently regurgitated and inhaled. The stomach should be kept empty with a naso-gastric tube until the infant is able to absorb adequate quantities of oral fluid.

4. Compatible blood must be available and a reliable intravenous transfusion set up before operation. Blood-loss and its replacement should be assessed, bearing in mind that the total blood-volume of a neonate is of the order of 45 c.c./lb. body-weight. A loss of more than 10 per cent (which in a 6-lb. baby would be about 27 c.c.) must be replaced.

5. Diagnostic exploration of the perineum to locate the blind distal bowel is a dangerous manœuvre. It is very easy to damage the pelvic nerves during such a dissection.

After-care must include repeated dilatation of the new anus as there is a strong tendency for this orifice to stenose, both in the low and high cases. The daily passage of a small stool does not exclude fæcal impaction, and abdominal and rectal examination is necessary to prevent the insidious development of colonic inertia (formerly called 'acquired' or 'secondary' megacolon). Daily dilatation with Hegar's dilators should, therefore, be performed for at least three months. By the third post-operative week a No. 14 dilator (about the size of an adult little finger) should pass with ease.

Low Anomalies.—

The Covered Anus.—The track is opened with a fine pair of scissors and cut back into the anal canal. Dilatation is carried out and any loose tags of skin excised.

Where no track is present, the A-shaped bar of skin is excised and by a perineal dissection the bowel is identified and opened. The skin and mucosa may be left unsutured, but we recommend that they be apposed with black silk. Routine dilatation follows.

The Stenosed Anus.—All that is required here is regular dilatation; it may be necessary to begin with the child anæsthetized. When the anus is microscopic, the opening may be eccentrically placed and a probe should be passed into the anal canal and the roof of skin excised before dilatation.

Anal Membrane.—This is easily ruptured with a pair of forceps; dilatation should follow.

The Ectopic Anus.—

Vulval and perineal ectopic: With the baby in the lithotomy position, the anus is enlarged posteriorly as far as the normal anal site by placing one blade of a pair of scissors within the anus and directing the other backwards along the perineal skin. As mentioned in the treatment of the covered anus, we recommend that the edges of mucosa and skin be sutured with black silk. This 'cut-back' is in effect an enlargement of the anus by longitudinal incision with transverse suture.

Vestibular ectopic: Two methods of treatment are available. Denis Browne has recommended the cut-back manœuvre as described above; this produces a continent bowel, but the close proximity of the anal and vaginal orifices may later be æsthetically unpleasant. Alternatively, posterior transplant may be undertaken. This may be postponed until the child

is 4 years old, or attempted earlier within the first 9 months of life. Should dilatations not be sufficient to prevent fæcal retention, initial cut-back does not preclude later transplantation. The operation is described in detail in the next section.

Vaginal ectopic: The treatment of choice is undoubtedly the formal transplant of the anus. The merit of operation in the first 9 months of life is that the subsequent dilatations are carried out while the child is still an infant, with less upset to the child and her mother. Further, the insertion of the dilator into the new anus simulates in some respects the passage of a stool, establishing in the child at an early age the reflex of opening her bowels through the new orifice; colonic inertia is less likely to develop. Against early operation is the difficulty of dissection within the infantile vagina.

Details of Operative Management of Anal Transplantation (*Fig.* 62).—With the infant in the lithotomy position, the vulva is held apart by means of a Joll's thyroid retractor. The mucosa of the vagina

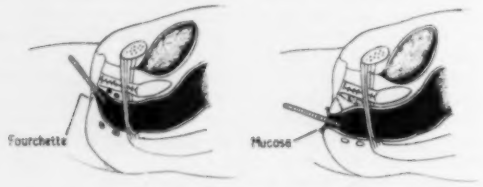

FIG. 62.—Vestibular ectopic anus.

is incised around the anus, thereby separating the epithelium of the two channels. To aid dissection, a rubber tube of about the same diameter as the anal canal is passed into the canal for a short distance and the edges of the anal mucosa sutured to it. The dissection is continued around the anal canal below the pelvic floor until sufficient bowel is freed. An ellipse of skin is then excised at the proposed site of the new anus and a canal fashioned in the fibrofatty tissue of the perineum down which the tube and anal canal are passed. The anus is fixed in its new site by one or two catgut sutures from bowel wall to the deep perineal tissues; a further stitch is inserted to re-form the perineal body and the mucosa is stitched to skin with interrupted black silk sutures. It is important to leave a wide bridge of normal skin between the original and new site of the anus, so a midline perineal incision should be avoided. It is not necessary to close accurately the defect in the posterior vaginal wall.

High Anomalies.—

Anorectal Agenesis in the Male.—Treatment is required for relief of the intestinal obstruction, and although opinions vary as to whether this should be palliative, or whether an attempt should be made at this time to achieve the final definitive result, we favour the latter course. Arguments as to the fitness of the baby to withstand radical surgery are valid when there is an associated major anomaly or when the baby is premature. In these circumstances, or when operating or nursing facilities are limited, a temporary loop colostomy should be performed in the proximal transverse colon, so that subsequent operation on the lower bowel may be carried out unhampered. Care should be taken to suture the bowel both to peritoneum and skin, as prolapse is common (Moore and Lawrence, 1952a).

The following are the courses of action which have been adopted in this series:—

1. Laparotomy, division of recto-urethral fistula, and transverse colostomy, the definitive rectal pull-through being performed later.
2. Laparotomy, division of recto-urethral fistula, and abdomino-perineal pull-through of the rectum in one stage.
3. Division of the fistula and rectal pull-down via the perineal route only.
4. Division of the fistula and rectal pull-down via a sacral approach.
5. Simple colostomy.

1. *Laparotomy and division of recto-urethral fistula with colostomy*: Prior to operation a urethral catheter

FIG. 63.—Anorectal agenesis.

is passed, which may at first enter the rectum (confirming the presence of a fistula). Laparotomy is performed through a transverse subumbilical incision, using cutting diathermy to minimize blood-loss during division of the abdominal muscles. The bladder rises high in the abdomen of the newborn baby and the urachal remnant or median umbilical ligament is short; this and the recently obliterated umbilical arteries are divided individually between ligatures and the peritoneum opened. The distended rectal pouch presents in the wound and further dissection is facilitated if aspiration is performed through a small colotomy. The peritoneum is then incised as low down on the anterior surface of the rectum as possible and all subsequent dissection is made close to bowel wall. Scott (1959) has described the distribution of the pelvic splanchnic nerves, both in the normal pelvis and in 4 cases of anorectal agenesis; their proximity to the distended blind bowel renders them especially liable to damage at this stage of the dissection. Traction on the urachal remnant will lift the bladder out of the pelvis and enable the recto-urethral fistula to be identified; this is transfixed and divided and the rectum oversewn. The abdomen is closed and a transverse colostomy performed.

2. *Division of recto-urethral fistula and abdomino-perineal pull-through* (*Fig.* 63): After division of the recto-urethral fistula, the lower bowel is mobilized; it may be necessary to divide one or two small vessels in the free edge of the sigmoid mesocolon to gain adequate length for the pull-through. The pelvic floor usually appears as a simple sheet of fibro-muscular and fatty tissue, and it is on the sphincteric

action of the muscle in this tissue that future continence depends. The puborectalis sling, undoubtedly the most important part of the levator ani with regard to continence, is, in the absence of the rectum, passing around the prostatic urethra. The new passage to be created through the pelvis must lie anterior to this sling and it is, therefore, formed by passing a pair of curved forceps downwards and forwards, keeping close to the urethra, and then following the curve of the pelvic outlet to the site of the future anus where the perineal skin is indented from above. When an ellipse of skin has been excised, the pathway for the new rectum and anal canal is completed. This is now enlarged with Hegar's dilators up to size 15, ensuring that an adequate passage is achieved with minimal risk of damage, not only to the pelvic splanchnic nerve-supply to the bladder, but also to the poorly differentiated pelvic floor. The bowel is drawn through, several deep catgut sutures inserted to anchor its wall to the fibrofatty tissue, and after careful suture of mucosa to skin with silk the new anus and anal canal are dilated. Gentle daily dilatations should be carried out post-operatively, at first with Hegar's dilators as it is some days before even the adult fifth finger can be passed without splitting the mucosa. Excoriation of the buttocks may develop post-operatively and prophylactic treatment with a barrier cream should be routine.

3. *Perineal dissection and pull-down*: Through a midline perineal incision blunt dissection is carried through the ill-defined tissues of the pelvis until the rectum is reached. This is freed from its loose attachments, the recto-urethral fistula defined and divided between ligatures, and the bowel mobilized sufficiently to allow suture to the perineal skin without tension. This and the following approach have now been abandoned.

4. *Sacral approach* (Stephens, 1953b): With the baby in the knee-elbow position, a midline incision is sited to allow detachment of the coccyx from the sacrum. The pelvic floor is held depressed by a self-retaining retractor and access gained to the recto-urethral fistula above the pelvic floor and below the peritoneum. Following division of the fistula and mobilization of the rectum, a pathway through the levator sling is fashioned and the bowel pulled down through the incision. The coccyx is replaced and skin closed around the new anus.

5. *Simple colostomy*: This should be carried out in male children as a temporary measure only because, by leaving the recto-urinary fistula intact, recurrent urinary infection may result, or urinary calculi may form in the blind distal loop of bowel.

In the analysis of results (*see below*) it will be seen that the outcome does not differ appreciably in the two principal forms of treatment (1 and 2). However, the authors favour abdomino-perineal pull-through as a primary procedure for the following reasons:—

a. The fistula is better visualized through the abdominal approach as the neonatal pelvis is relatively shallow, and the pelvic splanchnic nerves can be protected to the maximum degree during the pelvic dissection.

b. Following colostomy and division of the fistula the defunctioned loop of bowel retracts from the pelvis into the abdomen. Later pull-through has on occasions been rendered difficult by a relative shortness of the distal bowel and its vessels, as well as by post-operative adhesions.

c. There has been a tendency for colostomies to prolapse in the infant.

d. With later pull-through, the older infant resents repeated dilatation, making this very necessary manœuvre more difficult for the parents.

e. The older infant has been likely to develop more excoriation of the buttocks in the post-operative phase than has the neonate, with added risk of perianal sepsis, perhaps leading to fistula-in-ano.

f. Both the perineal and sacral approach to the fistula are more difficult technically. Recurrent fistula formation resulting either from incomplete division or damage to the bowel during mobilization has been more liable to occur and more difficult to treat following the perineal operation.

g. A definitive operation performed in the neonatal period restores the baby immediately to as normal an anatomical state as possible.

Anorectal Agenesis in the Female.—The same approaches are applicable to the female, and we favour the same initial definitive operation. In certain circumstances, however, choice of operation may be influenced by the absence of communication of the bowel with the urinary tract, enabling simple colostomy to be performed in the first instance without risk of subsequent urinary infection.

Rectal Atresia.—Diagnosis may not be established until laparotomy for intestinal obstruction. The blind proximal end of rectum is freed from its attachment to the pelvic floor and mobilized to provide sufficient length to reach the perineal skin. From below a Hegar's dilator is held against the apex of the blind distal pouch, which is then opened from above by a cruciate incision. The upper rectal pouch is drawn through, opened, and its edges sutured to the perianal skin.

Methods of Treatment in this Series.—Infants with low anomalies were in most instances treated by the methods described earlier.

1. Seventy-six cases (two-thirds of the total) of anorectal agenesis were referred in the first few days of life, and were treated as follows:—

	Total	*Deaths*
a. Abdomino-perineal pull-through, and division of fistula if present	33	9
b. Colostomy, with or without division of fistula	36	20
c. Perineal dissection	3	2
d. Laparotomy only	1	1
e. No operation	3	3

On one occasion laparotomy at 48 hours revealed gross peritonitis resulting from leakage of meconium through a perforation in the blind pouch of the rectum. This has not been found in any other case of anorectal agenesis, although failure to recognize the anomaly often delayed treatment until the third or fourth day of life. In 3 babies no operation was performed; 1 was a 2-lb. mongol with duodenal atresia also, 1 had absent abdominal musculature and severe talipes equinovarus, and the third died shortly after operation for œsophageal atresia.

The high proportion of deaths in the second group is due to the number of infants in this group in whom other abnormalities or illness made a major definitive operation unwise or unnecessary.

Subsequently the 16 survivors in this group who had had a primary colostomy were treated by:—

	Cases
Abdomino-perineal pull-through	14
Perineal pull-down	1
No further operation	1

The 1 child who has had no further operation is a mongol, although it is of interest that another mongol who has had a secondary pull-through carried out at the parents' request has had a result which they far prefer to a colostomy. There were no operative deaths.

2. The remaining 38 children with anorectal agenesis who were referred for further opinion had been treated initially by:—

	Cases
Colostomy	27
Perineal dissection	9
Urethral cut back	1
Abdomino-perineal pull-through	1

One male child had been mistakenly thought to have a low anomaly and the urethra had been cut back in an attempt to locate the anal canal.

These were further treated by:—

	Cases
Abdomino-perineal pull-through	17
Perineal dissection	14
Sacral approach	2
Left with permanent colostomy after division of recto-urethral fistula	1
Left with permanent colostomy following unsuccessful attempt at pull-through	1
No further operation	2
Refashioning of anus	1

The one infant who had a refashioning of the anus had developed anal stenosis following an abdominal pull-through operation. The only death in this group was caused by suppurative pyelonephritis in a solitary kidney.

Results of Treatment.—It has not been possible to trace all the children with low anomalies for adequate follow-up. Of the 148 for whom there are complete records, 128, or over 85 per cent, have normal bowel function. The results, according to the various types of anomaly, are set out in *Table IV*. A result is considered *good* when bowel control is normal without the use of regular laxatives; *fair* when continual supervision is needed to avoid recurrent constipation or anal stenosis—these children are usually being maintained on laxatives and suppositories; and *poor* when a state of severe colonic inertia or incontinence exists. The high percentage of good results has been achieved only by continual supervision, and many of these children spent some time in the *fair* category before normal function was gained. Re-stenosis of a previously dilated or cut-back anus often occurs; it is more liable to occur in the cut-back anus than in the stenosed anus at the normal site. Of the 20 *fair* or *poor* results, 10 can be directly attributed to the abnormality only being recognized by the onset of colonic inertia or overflow incontinence. This is more liable to occur in the vestibular ectopic anus and the stenosed anus as the anus in these two conditions is usually sufficiently large to allow the passage of a daily stool for some weeks or months; in the vulval ectopic anus there is usually more stenosis and the abnormality is noticed earlier. This colonic inertia was of such severity that rectal biopsy in 6 instances and barium enema in 2 was required to disprove the coexistence of Hirschsprung's disease. This combination of congenital abnormalities, although reported (Brayton and Norris, 1958), has not been found in any case in this series.

Examination of the older male child who has been 'cut back' for a covered anus usually shows an apparently normal anus and anal canal with a good external sphincter and a normal puborectalis sling. In the female the cut-back vulval or perineal ectopic anus results later in a normal-looking perineum, the two orifices which were closely approximated at birth becoming gradually separated by the development of a 'perineal body'. This separation does not occur in the similarly treated vestibular ectopic anus.

Anal transplant has been carried out in 8 children with a vestibular ectopic anus, 4 previously having had a cut-back in infancy, and in 3 with a vaginal ectopic anus. It has produced a good result, both functionally and cosmetically in all cases, but 2 children developed a post-operative rectovaginal fistula and required a colostomy and further repair before this good result was achieved. These fistulæ were caused by insufficient mobilization of the terminal bowel, which led first to tension on the new mucocutaneous suture line and then to its retraction.

Of the 114 cases of anorectal agenesis, 69 survivors have had operations which provided an anus at the normal site; 36 of the remainder died from causes which will be discussed later. Nine children still have colostomies; 4 will be permanent and 5 await further operation. The analysis in *Table V* of the present condition of these 69 children who have a normally situated anus has been based on hospital records, replies to questionnaires sent to parents, and, in many cases, by personal examination. Most of the children attend hospital regularly, enabling a clear impression as to the outcome to be gained. In the questionnaires we attempted to determine the continence of bowel and bladder, the age at which this was gained, and the ability of the child to lead a normal life.

A result has been regarded as *good* when the child is continent of fæces and urine, has his bowels

Table IV.—Results of Treatment of Low Anomalies

Type	*Total*	*Deaths*	*No Follow-up*	*Follow-up*	*Good*	*Fair*	*Poor*	*Average Length of Follow-up*
The covered anus	53	3	8	42	37	5	—	3·1 yr.
The ectopic anus:—								
1. Perineal and vulval	57	2	13	42	39	1	2	3·6 yr.
2. Vestibular	33	3	3	27	20	6	1	5·6 yr.
3. Vaginal	8	—	—	8	7	1	—	4·25 yr.
The stenosed anus	38	3	7	28	24	4	—	3·0 yr.
Anal membrane	3	—	—	3	3	—	—	2·4 yr.
	192	11	31	150	130	17	3	

open spontaneously and regularly, and appears to have some degree of rectal sensation in that a call to stool is recognized, and soiling is only an occasional accident. A *fair* result is one in which the child is continent of fæces, except when these are unusually loose, although soiling may commonly occur, and in whom laxatives or suppositories are often required.

Table V.—Results of Treatment of Anorectal Agenesis

	Total	No Follow-up	Good	Fair	Poor	With Colostomy	
						Better	Equiv.
Abdominoperineal pull-through at birth	24	5	7	9	3	16	3
Colostomy at birth. Abdominoperineal pull-through later	29	—	7	14	8	24	5
Colostomy at birth. Perineal dissection later	8	—	4	2	2	7	1
Perineal operation at birth. Further perineal operations later	7	1	2	2	2	4	2
Colostomy at birth. Sacral approach later	1	—	1	—	—	1	—
	69	6	21	27	15	52	11

Some children whose bowel function is good but whose control of micturition is impaired have been included in this category. A *poor* result is one in which the child has virtually a perineal colostomy, having little or no bowel control or sensation.

Finally each child's state has been compared with that of a permanent abdominal colostomy, against which the result must be assessed, this being the only alternative treatment. Although several children have been judged *Poor* results, they are nevertheless considered to be better than they would be with an abdominal colostomy.

Rectal Atresia.—Two of the 3 surviving children who had rectal atresia are continent and now have a normal bowel habit at 9 and 2 years respectively. The third, whose bowel was pulled down via a sacral approach, has normal control of his bowel but is incontinent of urine.

Complications of Treatment.—Colonic inertia, which has been discussed in relation to the low anomalies in the previous section, occurs also as a complication of the treated high anomaly. It may again be due to stenosis of the new anus following inadequate or excessive dilatation—for this produces scarring and therefore re-stenosis—but here there is also absence of the distal rectum and therefore of the sensory side of the reflex arc subserving defæcation. Long bowel training is required and in some cases it seems that as the child grows older and is better able to understand his disability increased control results without any palpable change in the puborectalis sling. If colonic inertia develops, laxatives and enemata are of little use owing to the atony of the bowel wall. The bowel must be emptied by manual evacuation of fæces and colonic washouts and as it regains its tone laxatives and suppositories, of which dulcolax (diacetoxy-diphenyl-pyridyl-methane) has proved most satisfactory, may again be used.

Most of the complications have occurred following treatment of the high abnormalities; urinary complications were the most frequent. Those which have been found are:—

1. Recurrent urinary infection has been the most common of all complications. Its causes have been multiple, viz., associated congenital abnormalities of the urinary tract; bladder-neck obstruction; recurrent or in some instances initially unrecognized recto-urethral fistula; incontinence due to sacral agenesis and its associated nerve involvement; and stasis, and in one instance stone formation, in a diverticulum of the posterior urethra due to high division of the recto-urethral fistula. In some older children a recto-urethral fistula has been discovered only after an attack of urinary infection; there is little doubt that in some of these the fistula was closed at birth and only later became patent. Recurrent urinary infection has been found associated with dilatation of the upper urinary tract on excretory pyelography. On control of the infection, for example by division of a recto-urethral fistula, the dilatation has disappeared. Infection caused stone formation in 2 children who had vesical calculi. Another child, who was suspected of having vesical calculi, was found to have stones in the blind loop of bowel distal to the colostomy, the urine having leaked back through a patent recto-urethral fistula.

2. Bladder-neck obstruction has probably been secondary to damage to the pelvic splanchnic nerves during the dissection of the bowel or its subsequent pull-through. Retention has led to recurrent urinary infection and the condition has been treated by bladder-neck resection in 2 children and Y–V-plasty (Williams, 1958) in another 2 cases.

3. Stricture of the posterior urethra has caused urinary obstruction. During operation traction on the blind loop of bowel readily displays the fistula, but also tents the urethra and renders it liable to damage by the transfixion stitch.

Complications referable to the bowel itself have been:—

1. Prolapse of the colostomy, which is more common in children than adults. The incidence of this complication has been decreased by always suturing the bowel both to peritoneum and abdominal wall.

2. Breakdown of the anastomosis following closure of the colostomy. Faulty technique may have played a part in this, but functional obstruction due to the inability of the distal bowel, defunctioned since birth, to respond to normal demands may have been responsible.

3. Rectal prolapse has more often followed a primary than a secondary abdominal pull-through operation, owing to greater ease of mobilization of the bowel in the former. Secondary trimming has been required in 10 children.

4. Anal stricture has followed breakdown of the suture line between bowel and perineal skin. This has been more frequent in children who have had a secondary pull-through operation.

5. Recurrent recto-urethral fistula has occurred in 10 children in whom a definitive operation had already been performed. Seven had had a perineal pull-down and 3 abdominal pull-through operations. Two of the 3 recurrences following the abdominal procedure were closed by perineal dissection at the first attempt, but only 3 of the 7 recurrences following the perineal pull-down were repaired by one operation.

6. One child has suffered from recurrent pelvic abscesses following an abdominoperineal pull-through operation. It has not been possible to demonstrate a fistulous connexion between the bowel and these abscesses, which extend upwards towards the peritoneal cavity, but it is assumed that one must exist.

Amongst the more general complications there have been 4 children who have required laparotomy for small-bowel obstruction due to post-operative adhesions; all made an uneventful recovery. Post-operative sclerema neonatorum has been the sole cause of death in 1 infant and a contributing factor in 2 others. Factors which have predisposed to sclerema have been prematurity, infection, and probably a low body temperature. All major neonatal operations in the last few years have been covered by prophylactic antibiotics and, owing to the inefficient temperature-regulating mechanism of the newborn baby, temperature loss during, as well as before and after, operation should be guarded against (Gough, 1960). Severe unexplained hypochromic anæmia has developed post-operatively in several children; hæmoglobin levels of 40–60 per cent have responded to the prolonged administration of oral iron.

MORTALITY AND CAUSES OF DEATH

The total number of deaths in the series was 58; 47 of these were in cases of the high and 11 in cases of the low anomaly. The overall mortality-rates were therefore 35·9 per cent and 5·7 per cent respectively.

Of more interest is the mortality-rate of the common high anomaly of anorectal agenesis which is shown in *Table VI* as 31·6 per cent, representing 36 deaths in a total of 114 cases. However, as previously mentioned in the section on treatment, 38 children had been referred following initial treatment elsewhere, and 1 of these died following a later operation. There were therefore 76 children with anorectal agenesis seen in the neonatal period at Great Ormond Street and 35 of these died—a mortality-rate of 46 per cent. This formidable figure is attributable to the high incidence of severe associated anomalies, no fewer than 24 of these 35 had other lesions such as congenital heart disease,

Table VI.—MORTALITY

Anomaly	Cases Total	Operative or Immediate Post-operative	Others	Mortality	
				Total	Percentage of Individual Total
High:					
Anorectal agenesis	114	18	18	36	31·6
Rectal atresia	5	2	—	2	40·0
Cloaca	9	1	5	6	66·6
Ectopia cloacæ	3	1	2	3	100·0
	131	22	25	47	
Low:					
Covered anus	53	—	3	3	5·7
Ectopic anus:					
Perineal vulval	57	—	2	2	3·5
Vestibular	33	—	3	3	9·0
Vaginal	8	—	—	—	—
Stenosed anus	38	—	3	3	7·9
Anal membrane	3	—	—	—	—
	192	—	11	11	
	323	22	36	58	

œsophageal atresia, or renal abnormalities which were themselves the cause of death. In the low anomalies, too, it was the associated abnormalities which caused 8 of the 11 deaths, 1 other dying of bronchopneumonia and 2 dying of unknown causes.

In *Table VI* the numbers of deaths in each anomaly are listed. Operative deaths include all infants who died at operation or before discharge from hospital; other deaths were due usually to the late effects of associated anomalies. *Table VII* lists the causes of deaths which were known in all except 3 of the high cases and 2 of the low.

DISCUSSION

Reports in the literature concerning the treatment of anorectal abnormalities have been increasing over the past ten years. Apart from the notable contributions by Denis Browne (1950, 1955) and Stephens (1953a, b), most of these reports have been from North America. The standard text-books of pædiatric surgery have also long been those of Ladd and Gross (1941), Gross (1953), and more recently that of Swenson (1958). The larger series of cases have been published by Moore and Lawrence (1952b) 120 cases, Bacon and Sherman (1952) 111 cases, Bill and Johnston (1958) 70 cases, and Brayton and Norris (1958) 93 cases. Bill and Johnston have used a classification based on Keith's embryological theories, whilst Brayton and Norris have used Ladd's classification which divides the abnormalities into four types (1–4).

Ladd's Type 3 cases include examples of both the low and the high anomaly in our classification,

e.g., the covered and vestibular anus and anorectal agenesis. We have shown how great a difference there is in the prognosis between the two main groups, and their combination under Type 3 in a well-documented follow-up such as that of Brayton and Norris makes comparison impossible between their series and the present one. These authors did, however, conclude that in Type 3 cases a primary definitive operation is the treatment of choice, and we agree with this conclusion both for the high and low anomalies.

Table VII.—Causes of Death

	Cases
Anorectal Agenesis:—	
Congenital heart disease	8
Renal hypoplasia or infection	3
Œsophageal anastomotic leak	2
Leak from colostomy or rectal pouch	6
Bronchopneumonia	5
Adrenal hæmorrhage	1
Agenesis of bile-ducts	1
Aspiration asphyxia	2
Gastro-enteritis	1
Cytomegalic inclusion disease	1
Sclerema neonatorum	1
Cause unknown	3
No operation due to multiple abnormalities	2
Total	36
Rectal Atresia:—	
Prematurity and sclerema neonatorum	1
Anastomotic leak and sclerema neonatorum	1
Total	2
Cloaca:—	
Congenital heart disease	1
Renal hypoplasia or infection	3
Gastro-enteritis	1
Post-operative infection	1
Total	6
Ectopia Cloacæ:—	
Multiple abnormalities Total	3
Covered Anus:—	
Congenital heart disease	2
Bronchopneumonia	1
Total	3
Ectopic Anus:—	
Renal agenesis	1
Congenital heart disease	1
Bronchopneumonia	1
Hæmorrhage from Meckel's diverticulum plus bronchopneumonia	1
Unknown	1
Total	5
Stenosed Anus:—	
Congenital heart disease	1
Agenesis of bile-ducts	1
Unknown	1
Total	3

SUMMARY AND CONCLUSIONS

1. A series of 323 children born with congenital abnormalities of the anus and rectum has been presented. The most important factor in differentiating these abnormalities and in deciding upon treatment and prognosis is whether the termination of the bowel is above or below the pelvic floor. Dependent upon this, the abnormalities have been grouped into 'high' and 'low' abnormalities and further classified, on a descriptive basis, into various types.

2. The basic embryology has been briefly stated and explanations of the various abnormalities reiterated. A cause for rectal atresia, based on the theory of vascular occlusion, has been suggested.

3. The incidence, diagnosis, and treatment of the various types of abnormalities in the series have been stated. The high anomalies formed 40 per cent of the series and the low 60 per cent. Of the total cases, 57 per cent were males and 43 per cent females.

4. The results and complications of treatment have been stated. The high incidence of associated congenital abnormalities, especially of the urinary tract, has been stressed.

5. The mortality-rate of children with anorectal agenesis first seen and treated in the neonatal period at Great Ormond Street was 46 per cent, the principal cause of death being an associated abnormality. The overall mortality-rate for high anomalies in the series was 35·9 per cent and for low anomalies 5·7 per cent.

6. It is concluded that the optimum treatment for the low anomalies of covered anus and perineal and vulval ectopic anus is the cut-back operation of Denis Browne (1950). Transplantation of the anus is preferable in the rare vaginal and the more common vestibular anus. Anal dilatation is an essential part of post-operative care, and in itself is adequate treatment for anal stenosis.

In the high abnormality of anorectal agenesis, the optimum treatment, in an otherwise fit baby, is an abdominoperineal pull-through operation as an initial definitive procedure. In the presence of other severe abnormalities a right transverse colostomy, and if possible division of a recto-urethral fistula, should be performed.

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LYMPHOSARCOMA IN CHRONIC ULCERATIVE COLITIS

WITH REPORT OF TWO CASES

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ALTHOUGH lymphosarcoma complicating chronic ulcerative colitis is often referred to in review articles, very few cases have actually been recorded in the literature. Bargen (1928), in a study of malignant disease associated with chronic ulcerative colitis seen at the Mayo Clinic, reported 2 cases of lymphosarcoma and 1 case of lymphatic leukæmia. These cases have been frequently referred to by other workers and by Bargen and his colleagues in numerous later publications. In the original paper (Bargen, 1928) only 1 case is described in detail. This was a man, aged 40 years, with a five-year history of chronic diarrhœa having three to fifteen bowel motions a day before the sudden onset of pain in the right iliac fossa. A firm, tender, nodular mass was palpable in the right lower quadrant of the abdomen and at operation a tumour was found in the cæcum which was considered to be malignant. An ileostomy was performed; two months later the mass was resected and the patient was alive and well a year after the operation. This tumour was an ulcerating lymphosarcoma of the cæcum without involvement of the regional lymph-nodes. Rankin and Chumley (1929) again referred briefly to these 2 cases in a paper on lymphosarcomas of the colon and rectum. The second case reported by Bargen (1928) was said to be an example of Hodgkin's disease of the transverse colon in a patient with chronic ulcerative colitis who died eighteen months later from generalized Hodgkin's disease.

Cattell and Boehme (1947) described the case of a woman, aged 26 years, who had suffered from ulcerative colitis for fifteen years and was treated by ileostomy. Three years later she died from massive hæmorrhage from the ileostomy and the rectum. At autopsy she had chronic ulcerative colitis with polyposis affecting the whole colon, an adenocarcinoma of the rectum, and a reticulum-cell sarcoma in the cæcum. Deposits of reticulum-cell sarcoma were found in the regional lymph-nodes, liver, and lungs.

Warren (1959) described a series of malignant lymphomas of the duodenum, small intestine, and colon seen at the Lahey Clinic, 2 of which were associated with chronic ulcerative colitis. One was in a patient whose ulcerative colitis had been quiescent for eight years and who complained of rectal bleeding and constipation. A left hemicolectomy and abdominoperineal excision of the rectum was performed for an adenocarcinoma of the splenic flexure and a malignant lymphoma of the rectosigmoid; this patient lived for approximately one year.

The second case was in a patient with long-standing ulcerative colitis who was treated by left hemicolectomy. Examination of the operation specimen showed a diffuse lymphoma involving the rectum. Postoperatively he developed multiple abdominal fistulæ and died six months later. These 2 cases were labelled lymphomas because the author was unable to classify them in any of the recognized groups of malignant tumours of lymphoid tissue.

Because very few cases have been reported and there is little information on this condition, we wish to set on record 2 cases of lymphosarcoma complicating ulcerative colitis, one seen at St. Mark's Hospital and the other at University College Hospital, London, and to draw attention to some of the pitfalls in diagnosis.

CASE REPORTS

Case 1.—Mrs. M. Z., aged 42 years, gave a past history of intermittent chronic diarrhœa, melæna, and weight loss over a period of eleven years (1943–54). For four years prior to her admission to St. Mark's Hospital in October, 1958, she had been in relatively good health apart from the two months before admission, when she complained of abdominal discomfort, loose stools, and diarrhœa. Examination revealed an indefinite, mobile, non-tender mass in the left iliac fossa; there was no palpable superficial lymphadenopathy and a chest radiograph appeared to be normal. The hæmoglobin was 12·3 g. per cent and the white blood-cells 9600 per c.mm., with a normal differential. A provisional diagnosis

of carcinoma complicating chronic ulcerative colitis was made and Mr. Lloyd-Davies performed a one-stage proctocolectomy with terminal ileostomy. At the operation one tumour was found in the sigmoid colon and another in the upper third of the rectum (*Fig.* 64) and both were thought to be carcinomas. The liver and spleen appeared to be normal and no enlarged lymph-nodes were seen. Six months after the operation she complained of dull pain in the left iliac fossa and examination revealed the presence of a mass which was considered to be a recurrent tumour. External irradiation was applied. This produced symptomatic relief and no tumour has been palpable since. When last seen, in January, 1960, she was in good health.

FIG. 64.—*Case* 1. Sigmoid colon and rectum. Chronic ulcerative colitis, with two separate primary lymphosarcomas.

EXAMINATION OF THE OPERATION SPECIMEN showed a normal terminal ileum and ulceration of the ileocæcal valve, with a small granulomatous polyp at this site. The colon was shortened, the mucosa was granular and congested, and in the sigmoid colon there was a tumour 10 cm. long which completely encircled the bowel. The cut surface was soft and greyish-white in colour, and the tumour extended right through the muscle coats into the surrounding pericolic fat. In the anterior quadrant of the upper third of the rectum, 5 cm. below the first tumour, there was an infiltrating growth 4 cm. in diameter, the cut surface of which appeared to be similar to the tumour in the sigmoid colon, but did not reach the perirectal fat. Microscopy showed a chronic ulcerative colitis in the healing phase affecting the whole colon. Close to the two tumours there was a considerable increase in submucous lymphoid tissue and no sharp transition between the two tumours and this tissue could be seen. Both were lymphoblastic lymphosarcomas, the cells varying from normal lymphocytes to cells twice their size. A few mitotic figures could be seen. In the rectum and sigmoid colon the muscle coats were destroyed by tumour cells. The muscle-fibres appeared to be eaten away by the tumour masses and there was a conspicuous absence of any surrounding fibrous reaction. Sections taken from seventeen hæmorrhoidal lymph-nodes were all free from involvement.

Case 2.—Mr. H. S., born 1894. He first began to suffer from diarrhœa, with blood in his stools, in December, 1943. A year later he was admitted to University College Hospital for examination and investigations. He was then passing about ten loose, blood-stained motions daily. There was some abdominal tenderness but no other abnormality was found; sigmoidoscopy showed a congested mucosa which bled easily when touched. Barium-enema studies on two separate occasions showed the typical appearances of a chronic ulcerative colitis and no pathogens were isolated from the stools. He was traced medically for ten months and discharged from hospital slightly improved. From 1945 to May, 1959, he continued to suffer from diarrhœa, having three to ten loose bowel motions daily, but in May, 1959, there was an exacerbation of his symptoms, with abdominal pains, increasing diarrhœa, and weight loss. A large, firm mass was palpable in the right iliac fossa and a barium enema showed this to be in the cæcum. There was no palpable superficial lymphadenopathy and a chest radiograph was normal. The hæmoglobin was 11.4 g. per

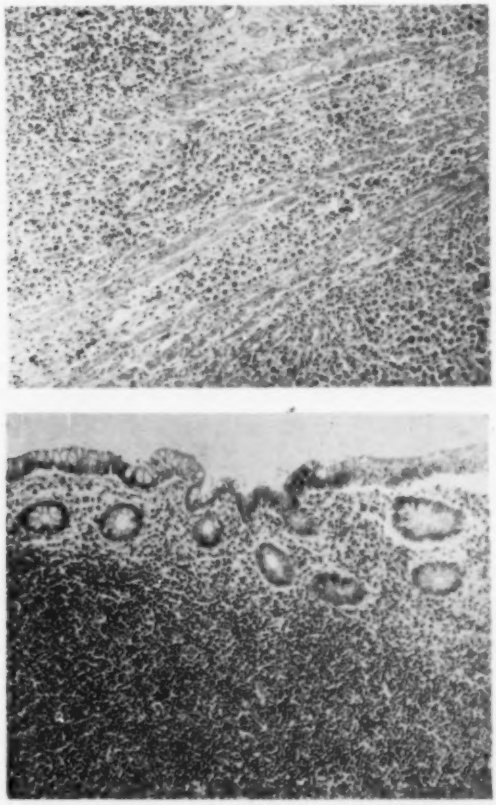

FIG. 65.—*Case* 2. Two photomicrographs showing a lymphoid tumour, of reticulum-cell type, in the submucosa and muscle coats of the ascending colon. (× 100.)

cent and the white blood-cell count was 11,800 per c.mm., with a normal differential.

He was admitted to University College Hospital with a provisional diagnosis of carcinoma complicating ulcerative colitis and a laparotomy was performed by Mr. A. J. Gardham on June 2. The presence of a large mass in the cæcum was confirmed and the remainder of the colon appeared shortened and rigid. No growth was apparent elsewhere. The liver and spleen appeared normal and the only enlarged nodes seen were those around the superior mesenteric vessels, close to the cæcal tumour. The nodes were soft to palpation and were thought to contain secondary tumour deposits. A palliative right hemicolectomy was therefore performed, and bowel continuity restored by side-to-side ileocolic anastomosis.

He made an uneventful recovery and was subsequently given a post-operative course of deep X-ray therapy. Following the operation he felt much better, put on weight, and suffered from only slight diarrhœa, but nine months later he was readmitted to hospital with a recurrence and at laparotomy a large growth was found in the transverse colon, just distal to the anastomosis. This was resected and found to be similar to the primary tumour removed nine months earlier. His post-operative progress was stormy, but at the time of writing he seems to be recovering satisfactorily.

EXAMINATION OF THE OPERATION SPECIMEN showed a normal terminal ileum, a large ulcerating tumour in the cæcum, two small plaques of growth in the ascending colon, and areas of healed chronic ulceration in the transverse colon. On sectioning, the cæcal tumour could be seen growing right through the muscle coats but there was no obvious invasion of the pericolic fat. The tumour extended downwards to involve the appendix. The plaques of growth in the ascending colon were confined to the mucosa and submucosa. Microscopy showed lymphoid tumours of reticulum-cell type (*Fig.* 65). The cells were large, with abundant, pale-staining, amphophilic cytoplasm showing a syncytial arrangement in some areas. The nuclei were large, ovoid, and slightly indented. Many bizarre nuclei were also seen throughout the tumours. The muscle coats were invaded and replaced by the tumour masses and no surrounding fibrous reaction was seen. Two out of four regional lymph-nodes taken for histology were found to contain secondary lymphoma. Sections of the colon away from the tumour areas showed the histological appearances of a chronic quiescent ulcerative colitis.

DISCUSSION

In all reported cases lymphosarcoma, like carcinoma, occurred in the late stages of ulcerative colitis, usually when the disease had burnt itself out and become quiescent. The development of lymphosarcoma was associated with the recurrence of symptoms seen in the earlier phases of the disease and the symptoms suggested the development of a malignant tumour in chronic quiescent ulcerative colitis. Clinically, radiologically, and at operation it may be impossible to distinguish a lymphosarcoma from carcinoma because carcinomas developing in chronic ulcerative colitis often have a bizarre appearance (Counsell and Dukes, 1952). Such carcinomas are occasionally multiple and may spread diffusely along the colon. The true nature of these tumours is usually not established until sections have been examined under the microscope. We agree with Warren (1959) that the finding of lymphosarcoma in chronic ulcerative colitis stresses the fact that long-standing ulcerative colitis, regardless of long periods of quiescence, is an invitation to malignant degeneration.

Lymphosarcoma is an unusual complication of chronic ulcerative colitis. In 352 operation specimens of part or all of the large intestine removed for ulcerative colitis which were examined in the research department of St. Mark's Hospital there were 16 carcinomas and only 1 lymphosarcoma. In a series of 663 patients suffering from ulcerative colitis, seen at the Gordon Hospital, London, there were 19 cases of large-intestinal carcinoma and no lymphosarcoma (Dawson and Pryse-Davies, 1959). Similarly, in 222 operation specimens removed from patients with ulcerative colitis at the Queen Elizabeth Hospital, Birmingham, there were 15 carcinomas (Slaney and Brooke, 1959) but no lymphosarcoma (Brooke, 1959).

Primary lymphosarcoma of the colon and rectum is, in itself, an uncommon disease, and at St. Mark's Hospital only 4 lymphosarcomas have been seen among 4595 malignant large-intestinal tumours during the period 1928–58 inclusive. Many of the cases recorded in the literature are, in fact, secondary involvement of the bowel in generalized disease. They were reported as primary bowel tumours because the earliest, or most important symptoms, were referable to the bowel or because the lesion in the bowel was larger and more impressive than the lesions seen elsewhere. To make the clinical diagnosis of a lymphosarcoma primary in the bowel, it is necessary to show that there is no obvious palpable superficial lymphadenopathy, that the mediastinal lymph-nodes are not enlarged as shown by chest radiography, that the liver and spleen appear free from tumour at the time of operation, and that the only lymph-nodes obviously affected are those in the immediate neighbourhood of the bowel lesion. A white blood-cell count will also help to exclude the possibility of a lymphatic leukæmia. If such strict and reasonable criteria are employed very few cases of primary lymphosarcoma of the colon and rectum have been recorded. We have been able to find only 19 reported cases where there was sufficient data on the clinical and pathological findings to be sure that we were dealing with a malignant tumour of lymphoid tissue primarily situated in the colon or rectum.

It is not possible to determine whether the association of lymphosarcoma and ulcerative colitis is significant or not, but the finding of such an uncommon disease on 7 occasions in cases of chronic ulcerative colitis may possibly have some significance and an association between these two diseases cannot be completely excluded. It is tempting to imagine that there might be some relationship between the repeated episodes of lymphoid hyperplasia seen in the quiescent phases of the disease and the eventual development of lymphosarcoma.

When malignant tumours of lymphoid tissue are multiple and involve long segments of the small or large intestines, the patient's symptoms can closely mimic those of ulcerative colitis. One patient was seen at St. Mark's Hospital with a history of central abdominal pains for several years, diarrhœa for one year, and melæna for six months. He was diagnosed as ulcerative colitis and treated with cortisone at another hospital. After an initial improvement he relapsed and was later admitted to St. Mark's Hospital for surgery. At operation the colon was normal but multiple small tumours were present throughout the jejunum and ileum; 30 cm. of

jejunum were resected and examination showed multiple lymphocytic lymphosarcomas in the submucosa, with some invasion of the underlying muscle coats. When such lesions are present in the colon, not only do the symptoms mimic ulcerative colitis, but barium-enema study may even suggest such a diagnosis (Ralston and Wasdahl, 1958).

In the healing phase of ulcerative colitis dense accumulations of lymphocytes, with some plasma cells, can be seen in the lamina propria and superficial submucosa (Lumb, 1958). These cells diffusely infiltrate the muscularis mucosæ with fragmentation of the muscle elements and it is possible that sections from such lesions might be misdiagnosed as lymphosarcomas by inexperienced observers. In the defunctioned colon or rectum these changes are even more pronounced. There is a dense lymphocytic infiltration with an increase in the number of follicles in the submucosa, and to a lesser extent in the subserous coat (Lockhart-Mummery, 1956). We agree with Stout (1955) that the criterion used to determine whether a primary lymphoid tumour in the bowel is benign or malignant should be whether or not the muscle coats have been invaded. If they have, the growth must be regarded as malignant. Azzopardi and Menzies (1960) have drawn attention to the characteristic appearances of lymphoid tumours invading the muscle coats. The destruction of the muscle coats is usually more complete than with carcinoma, there is a conspicuous absence of any surrounding fibrous reaction, and the muscle coats appear to be punched out by the tumours. Lymphocytes are occasionally present around the blood-vessels and nerves in the muscle coats in ulcerative colitis, but these infiltrations are slight and only tiny focal collections of cells can be seen. Destruction of the muscle coats is not a feature of chronic ulcerative colitis; in fact, the muscle coats are almost invariably thickened either as a result of hypertrophy or, more probably, because of the shortening of the colon.

The prognosis of primary malignant tumours of lymphoid tissue in the colon and rectum is not known. Too few examples have been recorded and most published cases are either secondary tumours or lack sufficient data for a critical study of this condition. The influence of ulcerative colitis on primary lymphosarcomas of the large intestine cannot, therefore, be determined, but the finding of recurrent growth in both these patients within a year hardly suggests a good prognosis.

SUMMARY

1. Lymphosarcoma is an unusual complication of chronic ulcerative colitis. Two cases of primary lymphosarcoma of the large intestine in patients with chronic ulcerative colitis are described and 5 similar cases reported in the literature are discussed.

2. Care must be taken to differentiate the dense accumulations of lymphoid tissue seen in the submucous and subserous coats of the defunctioned large intestine or in the healing phases of ulcerative colitis from true lymphosarcoma. The diagnosis of lymphosarcoma primary in the colon should not be made in the absence of invasion of the muscle coats.

3. The symptoms of diffuse lymphosarcoma of the intestinal tract may closely mimic ulcerative colitis and even barium-enema studies may suggest such a diagnosis.

4. It is suggested that there may be a significant association between lymphosarcoma and chronic ulcerative colitis.

ADDENDUM

Since the preparation of this paper both the patients have died. In neither case was a post-mortem performed, but both were noted to have masses which were presumed to be recurrent growth before death, and their progress was that of persons dying of malignant disease.

The first case died one year and nine months, and the second one year and two months, after the original operation, confirming the poor prognosis of this condition.

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NON-SPECIFIC ULCERATION OF THE CÆCUM*

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INTRODUCTION

THE importance of a thorough knowledge of the range of possible pathological processes occurring in any region of the body subjected to surgical exploration is self-evident. Since the right iliac fossa is the region of the abdomen most frequently explored it is clear that anyone engaging in abdominal surgery must be familiar with the less common (and therefore less well-known) lesions found in this region.

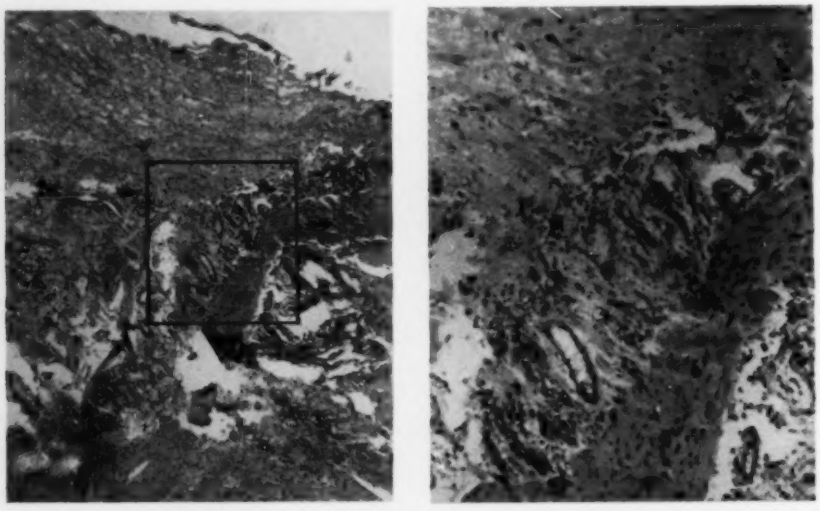
Non-specific ulceration of the cæcum is such a lesion. Reference to the literature would suggest that it is of considerable rarity as judged by the fact that less than 100 cases have been reported during the past 130 years. Moreover, reading the published case records leads one to believe that non-specific cæcal ulceration is a condition calling for extensive surgical excision, a conclusion which is not supported by the results of less extensive procedures employed in some of the cases reported in this paper.

When considering the natural history of a lesion such as non-specific ulceration of the cæcum, it is permissible (in the absence of more accurate information) to infer the sequence of events from a study of a small series of isolated observations which appear to represent different stages in the development of the condition. This line of argument bears greater conviction if the sequence of events which it suggests parallels the development of more commonly observed ulcers at other sites in the body.

Areas of non-specific cæcitis (typhlitis) are not infrequently observed at laparotomy, and it would seem that most of these areas settle down without progressing to ulceration (Emmett, 1954). *Case* 1 is an example of such a lesion.

CASE REPORTS

Case 1.—Miss L. V., 22 years of age, presented with malaise, fever, and colicky pain in the right iliac fossa of 48 hours' duration. Her temperature was 37·9° C., and examination revealed the typical signs of acute appendicitis.



A B

FIG. 66.—A, A photomicrograph of the biopsy taken from the edge of the cæcal ulcer in *Case* 3. The ulcer crater is seen to be filled with exudate consisting of fibrin and small round cells. (× 24.) B, A photomicrograph of the area indicated in A under higher magnification, showing the non-specific granulation tissue in greater detail. (× 64.)

However, at operation the appendix was normal and the only finding was an inflamed œdematous plaque 4 cm. in diameter on the lateral cæcal wall—palpation of which failed to reveal an ulcer crater. Appendicectomy was performed and the abdomen closed without drainage, following which the patient made an uneventful recovery.

However, on occasion, a lesion such as that described above may progress to ulceration, and if laparotomy is carried out at this stage in the disease process, a shallow ulcer may be palpable in the centre of an area of acute inflammation.

Case 2.—Miss I. M., 18 years of age, presented with the history and findings on examination typical of acute appendicitis. At operation the peritoneal cavity contained a little free fluid, the cæcum was reddened and had a readily palpable ulcer on its postero-medial aspect adjoining the ileocæcal valve. The adjacent lymph-nodes were enlarged and the appendix was normal. Appendicectomy was performed and the abdomen closed.

* This review was carried out whilst the author was holding a grant from the Aid-Cancer Council of Victoria.

Convalescence was uneventful and a barium enema one month later revealed no cæcal abnormality. (Similar cases have been reported by Bulmer (1947) and Horne (1955) in which an acute ulcer was detected at operation and in which the abdomen was simply closed. In both cases a barium enema was performed later and failed to reveal any abnormality of the cæcum.)

FIG. 67.—A photograph of the barium enema in *Case* 5 showing a stricture in the cæcum. Tenderness was elicited over this area which was considered to be inflammatory in origin. At laparotomy eight weeks later the lesion had almost completely resolved.

Case 3.—Mrs. P., 38 years of age, presented to her doctor complaining of pain in the right iliac fossa and a diagnosis of acute appendicitis was made. However, at operation the appendix was normal and there was an ulcer 3 cm. in diameter on the anterior aspect of the cæcum adjacent to the ileocæcal valve. The ulcer had a discrete raised edge which was readily palpable through the cæcal wall. A biopsy was taken from the edge of the ulcer. The patient made an uneventful recovery and remains well ten years later. Histological examination revealed a typical non-specific inflammatory process (*Fig.* 66).

Clearly an ulcer having formed may penetrate into the posterior abdominal wall, as has been described by Moore (1939), or may perforate, giving rise either to a local abscess (*Case* 8) or to general peritonitis.

Case 4.—Mr. S., 79 years of age, presented with general peritonitis, and laparotomy revealed a large ulcer of the cæcum with a 2-cm. perforation which permitted the free escape of bowel contents. It was appreciated that this lesion was a benign ulcer; however, as simple closure was not possible a right hemicolectomy was performed. He initially improved but later developed renal failure and died. Histological examination of the cæcal wall revealed a number of intramural abscesses and intense infiltration by macrophages and polymorphs.

On the other hand, the ulcer may heal, and, healing having occurred, the changes associated with repair will mask the histological features of the initial destruction process.

FIG. 68.—A photograph of a barium enema in *Case* 6 showing a filling defect in the cæcum. Preservation of the mucosal pattern over the involved area suggested an inflammatory lesion and this was confirmed at laparotomy.

Case 5.—Miss A. D., aged 45 years, presented to her doctor following a small hæmatemesis. She stated that she had suffered from lower abdominal discomfort for two years; that six years previously she had had an appendicectomy; and that she had received treatment for pulmonary tuberculosis twelve years previously. A barium meal disclosed no abnormality, but a barium enema revealed a persistent narrowing of the cæcum (*Fig.* 67), which was tender on palpation. It was accordingly suggested that the lesion in the cæcum was tuberculous, and following an 8-week course of anti-tuberculous drugs the cæcum was explored. At operation there was only a slight generalized thickening of the cæcal wall and no palpable ulcer or mass. Right hemicolectomy was performed and this was followed by an uneventful convalescence. On opening the operative specimen it was apparent that there was an area 3 cm. in diameter in which the normal mucosal folds had disappeared. Histological examination revealed only an area of submucosal fibrosis and some accumulation of small round cells as evidence of past inflammation; there were no histological features to suggest a tuberculous basis. The presence of a filling defect eight weeks prior to operation and the macroscopic and microscopic appearance of the specimen support the belief that the lesion was a non-specific cæcal ulcer.

Should the inflammatory process be less severe a chronic inflammatory mass may develop (Parker and Serjeant, 1957; Rosser, 1944).

Case 6.—Mr. W. M., 25 years of age, presented with six months' colicky lower abdominal pain, nausea, loss of 2½ stone in weight, and the passage of a small quantity of bright blood per rectum. Deep tenderness was present in the right iliac fossa and a barium enema revealed a filling defect in the cæcum. The radiologist considered a neoplasm to be the most probable diagnosis. However,

FIG. 69.—A photograph of the resected specimen from *Case* 6 (*Fig.* 68), showing the terminal ileum and cæcum opened along its anti-mesenteric border. An ulcerated area can be seen adjacent to the ileocæcal valve.

as the mucosal pattern was not completely obliterated, he did not rule out the possibility that the mass was inflammatory (*Fig.* 68). Laparotomy disclosed a large cæcal mass adherent to the posterior abdominal wall and enlargement of the adjacent lymph-nodes. A provisional diagnosis of carcinoma of the cæcum was made and a right hemicolectomy performed, following which the patient recovered uneventfully. (*Fig.* 69.)

Histological examination revealed a mucosal defect lined by hæmorrhagic granulation tissue in which there were many macrophages and polymorphs. This defect extended down to the muscularis which was infiltrated with small round cells and polymorphs (*Fig.* 70).

Case 7.—Mr. M. M., 37 years of age, had had an interval appendicectomy performed eight years previously and had suffered recurrent bouts of pain in the right iliac fossa for four months prior to presentation. Physical examination revealed slight tenderness and fullness in the iliac fossa and a barium enema disclosed an irregular narrowing of the cæcum, terminal ileum, and ascending colon.

FIG. 71.—A photograph of the resected specimen from *Case* 7, showing terminal ileum and cæcum opened to reveal an irregular lobulated mass arising from the cæcum and extending upwards to involve the ascending colon. Histological examination revealed necrosis of the mucosa although this was not apparent macroscopically.

FIG. 70.—A photograph of a histological section through the ulcer seen in *Fig.* 69 (*Case* 6). A mucosal defect lined by hæmorrhagic granulation tissue is seen extending down to the muscularis which is infiltrated with small round cells and polymorphs. (× 5.)

At laparotomy an inflammatory mass arising from the cæcum was found and a right hemicolectomy was performed. An uneventful convalescence ensued, and when last seen (three years after operation) he was very well. Examination of the specimen revealed thickening of the cæcal wall extending upwards to involve the ascending colon. The mucosal surface was irregularly lobulated and nodular, but macroscopically not ulcerated (*Fig.* 71). Histological examination revealed that the mucosa was necrotic over an area 4 cm. in diameter. The base of the ulcer was covered with fibrin and leucocytes and there was considerable endarteritis and accumulation of polymorphs and plasma cells.

Case 8.—Mrs. L. S., 34 years of age, had an abscess in the right iliac fossa drained six weeks before admission and for the two months prior to this operation had suffered from colicky abdominal pain and nausea. A firm tender mass, thought to be an appendicular abscess, was palpable in the right iliac fossa and was treated conservatively. As her symptoms failed to subside laparotomy was undertaken and a mass, considered to be neoplastic, was found in the wall of the cæcum. A right hemicolectomy was performed, from which the patient recovered uneventfully. On opening the operation specimen, the lumen of the bowel was found to be considerably narrowed by an ulcerating fungating mass 8 cm. in length arising from the cæcum and adjacent ascending colon. Firm white tissue replaced the wall and extended out into the surrounding fat, and the adjacent lymph-nodes were replaced by similar tissue (*Fig.* 72). Histological examination confirmed the presence of areas of ulceration of the mucosa and revealed gross inflammatory infiltration of the mucosa and submucosa. In some areas polymorphs were numerous but in most parts lymphocytes predominated. Section of an adjacent lymph-node also revealed typical inflammatory changes.

It is of interest to note at this juncture that in these last three patients the ulcers were multiple and, furthermore, the changes were not confined to the cæcum but had extended to involve the ascending colon and terminal ileum.

REVIEW OF THE LITERATURE

Although Cruveilhier is credited with first describing non-specific ulceration of the cæcum in 1832, it is doubtful whether he recognized this condition as a specific entity. His treatise on ulceration of the intestine (*Maladies des Intestins, Anatomie Pathologique*, 1835) is devoted almost entirely to tuberculosis and only in conclusion does he mention that on occasion he has seen ulceration of the small and large bowel occur in patients in whom there was no evidence of tuberculosis.

In 1928 Barron reviewed 50 cases of ulcer of the colon, and by 1941 Barlow was able to collect 78 cases from the literature. These publications included ulcers at all sites in the colon, and of the total number reported half were cæcal ulcers. However, it was appreciated that many of the earlier cases were instances of ulcerative colitis or diverticulitis or were of other known aetiology (e.g., the case reported by Greenhow in 1848 where diffuse colonic ulceration followed the administration of mercuric chloride).

While it is apparent that cases such as this have no place in any review of non-specific cæcal ulcer, this lesion was nevertheless recognized as a clinical and pathological entity by early writers, and St. Bartholomew's Hospital Report of 1887 included 2 cases of cæcal ulceration progressing to perforation and fatal peritonitis.

AETIOLOGY

Lack of precise information concerning the factors responsible for the development of non-specific cæcal ulceration has permitted the growth of a large number of doubtful theories of aetiology. Mechanical trauma, chemical damage (Cameron, 1939), decreased vascularity of the cæcal mucosa (Wilkie, 1937; Cameron, 1939), dietary factors (Harrison, 1940), inflammation in a cæcal diverticulum (Fox 1951), and even habitual constipation (Kerr, 1935) have been put forward as causative factors.

Many authors have drawn a comparison between this lesion and peptic ulcer (Barron, 1930; Cameron, 1939; Barlow, 1941), finding support in the similarity between cæcum and duodenum, both of which admit fluid through an orifice guarded by a sphincter.

FIG. 72.—A photograph of the resected specimen from *Case* 8 showing terminal ileum and cæcum. An ulcerating fungating mass is seen arising from the cæcum and there is infiltration of the cæcal wall by dense inflammatory tissue.

The feature of non-specific cæcal ulcer which seems to have impressed writers most is the close relationship which the site of ulceration is said to have to the ileocæcal valve (Cameron, 1939; Harrison, 1940.) However, as comparable ulcers do occur elsewhere in the colon (Katifi, 1956) and even in the blind loop of an intestinal anastomosis (Clawson, 1953; Wangensteen, 1955), it is highly unlikely that any local factor in the ileocæcal region is of importance in the production of cæcal ulcers. Moreover, in the absence of any characteristic histological appearance it is doubtful whether cæcal ulceration even deserves to be regarded as a specific entity.

On occasion there may be considerable difficulty in distinguishing other varieties of inflammatory process in the ileocæcal region and it may well be that the non-specific cæcal ulcer is related to segmental colitis or even to Crohn's disease.

TREATMENT

It has been pointed out that the fate of a cæcal ulcer is comparable with that of ulcers occurring elsewhere in the gastro-intestinal tract. It is difficult to estimate how frequently healing occurs, but it is possible that some cases of "mild subsiding appendicitis" may be in actual fact cæcal ulcers which heal completely (Parker and Serjeant, 1957).

On reviewing the literature the impression is gained that non-specific ulceration of the cæcum is associated with a high mortality and that any suggestion that healing may occur is untenable. This viewpoint is not limited to the early writers; Rabinovitch, Rabinovitch, and Lipton in 1958 stated that acute ulceration of the cæcum is a progressive lesion and that perforation will occur in all cases. Furthermore, Lipton and Reisman (1951) from their review of the

literature concluded that no case has survived without operation and estimate the operative mortality to be 40 per cent. Similar figures have been quoted by Cameron (1939) and Harrison (1940). However, in evaluating these statements it must be remembered that a positive diagnosis of cæcal ulcer can only be established at operation or autopsy, and hence any series will tend to include a significant proportion of fatal cases.

Non-specific ulceration of the cæcum is an operative diagnosis and the surgeon may be confronted with this lesion at the following stages of its development:—

1. Chronic Inflammatory Mass.—Such a mass may be detected on clinical examination, by a barium enema, or at laparotomy. Resection will be indicated both on the merits of the mass itself and because the precise diagnosis will be uncertain, and will remain so, until the resected specimen is examined post-operatively.

2. Pericæcal Abscess.—This may be diagnosed either pre-operatively or at laparotomy (the case having probably been regarded as an appendicular abscess and treated conservatively). At operation drainage of the abscess should be undertaken and if a fæcal fistula subsequently develops appropriate treatment will be instituted.

3. General Peritonitis.—Laparotomy will reveal the causative benign cæcal ulcer which should be oversewn or resected depending on the local problems and the general condition of the patient.

4. Unperforated Ulcer.—The appropriate management of the complicated cæcal ulcer follows well-established general surgical rules. However, when faced with a simple unperforated ulcer many surgeons, fearing progression to perforation and considering it unlikely that healing will occur, have performed a right hemicolectomy. This attitude is no doubt due to the writing of previous authors who, impressed by the reported high mortality, have felt that the ulcer must either be resected or at least oversewn (Eagleson, 1952). (Right hemicolectomy has of course also been performed in some cases in which the benign nature of the lesion was not appreciated.)

Few cases have been recorded in the literature in which no attempt was made either to resect or oversew the ulcer, the surgeon being content with simple closure of the abdomen. (Bulmer (1947), Tagart (1953), Horne (1955), and De Camp and Penick (1956) have each reported 1 case.)

In view of the increased morbidity and mortality following hemicolectomy as compared with simple laparotomy, it is clear that one must critically evaluate the indication for such an extensive procedure. In the 3 cases referred to in this paper and in those collected from the literature in whom no definitive treatment was instituted an uneventful recovery followed in each instance.

In an uncommon condition such as this the frequency with which healing occurs is unknown; however, it is known that ulcers elsewhere in the gastro-intestinal tract do tend to heal. Furthermore, it is likely that many cases of cæcal ulcer pass undiagnosed and presumably heal, and that only the more gross examples of this lesion come to laparotomy. Thus it is apparent that the frequency with which healing occurs may be much greater than has hitherto been appreciated, and that right hemicolectomy is seldom indicated or justified in the treatment of the uncomplicated non-specific cæcal ulcer.

SUMMARY AND CONCLUSION

1. Eight cases of non-specific cæcal ulceration are described.

2. It is probable that this condition is more common than a review of the literature would suggest—most cases of this uncommon condition passing either unrecognized or unrecorded.

3. The various theories of aetiology are discussed and the probable natural history of this lesion is outlined.

4. It is pointed out that as the diagnosis of non-specific cæcal ulcer can be made only at operation or at autopsy the frequency of healing is unknown.

5. Review of the literature would suggest that perforation frequently occurs and that extensive surgical procedures are therefore indicated. This concept is not supported by the cases reported in this paper and a more conservative approach to the unperforated ulcer is therefore advocated.

6. Non-specific cæcal ulcer may mimic acute appendicitis—the most common of all acute surgical conditions—thus it behoves all who undertake exploration of the right iliac fossa to be aware of its existence.

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THE LATE RESULTS OF HELLER'S OPERATION IN THE TREATMENT OF ACHALASIA

By N. L. BROWSE and S. J. CARTER
BRISTOL ROYAL INFIRMARY

ACHALASIA of the cardia is a rare disease. The majority of papers present small personal series. Only five papers (Acheson and Hadley, 1958; Douglas and Nicholson, 1959; Ellis, Oben, Holman, and Code, 1958; Hawthorne, Frobese, and Nemir, 1956; Latreille and Michaud, 1955), considering just over two hundred and fifty cases in all, give detailed accounts of the results five to ten years following Heller's operation.

We found it necessary to have more information on our own long-term results when achalasia was discovered in an 8-year-old boy. A knowledge of the late results became of the utmost importance in deciding the correct treatment for so young a patient and so this follow-up was instigated.

Achalasia is a disease without physical signs. The diagnosis depends upon: (1) The symptoms (*Part I*), principally dysphagia and regurgitation; (2) The radiological appearances of the œsophagus (*Part II*). The follow-up was therefore based upon an assessment of the effect of the operation upon these two factors.

PART I. CLINICAL

Clinical Material (*Table I*).—

Number of Cases.—Fifteen cases of achalasia were treated by Heller's operation at the Bristol Royal Infirmary between 1948 and 1956. These have all been traced and interviewed.

Age.—The youngest was 13, the eldest 69 years old. The remaining 13 fitted into two age-groups: (1) A young group, 17–27 years (5 cases); (2) A middle-aged group, 45–55 years (8 cases).

Sex.—The ratio is 11 females to 4 males (3:1). It is interesting that in the young group the ratio is 1:1, whereas in the middle-aged group it is 8:1 in favour of the females. This may explain the varying reports of a higher incidence of the disease in females and may also indicate a difference in aetiology in these two groups.

Aetiology.—There was no common factor to indicate the cause of the disease. Four patients could remember having swallowing difficulties when young. One patient was definitely psychoneurotic. She was the only patient made worse by the operation and has been referred to a psychiatrist on two occasions. The remainder appeared to be emotionally stable and only two claimed that their disease began as a result of an emotional upset.

The Operation (*Modified Heller's Operation—Barlow*, 1942).—The œsophagus is washed out and emptied pre-operatively. An abdominal incision is made. The left lobe of the liver is retracted to the right after dividing the left coronary ligament. The cardia is displayed by dividing the peritoneum over the œsophago-gastric junction, assisted by downward traction on the stomach. An anterior extramucous œsophago-cardiomyotomy is then performed.

This operation was performed on 13 of the 15 patients. In 2 cases the approach was through a thoracic incision, but the same type of myotomy was performed. The average length of the myotomy was three to four inches. In *Cases* 5, 9, 13, and 14 the mucosa was accidentally divided and the œsophageal lumen opened. In each case the opening was closed with catgut stitches. This accident was not followed by any special post-operative complication.

The average stay in hospital, after operation, was fourteen days.

Table I.—CLINICAL MATERIAL

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Age at operation	24	20	49	22	27	52	46	13	22	47	46	54	54	69	52
Sex	M	M	F	M	F	F	F	F	F	M	F	F	F	F	F
Follow-up period (years)	12	11	10	10	9	9	9	8	8	8	7	6	6	5	4
Incision {A: Abdominal T: Thoracic	A	A	A	T	A	A	A	A	A	A	A	A	A	T	A
Length of myotomy (inches)	6	2	3	4	2	4	4	3	?	3	2	?	?	4	2
Days in hospital	6	13	10	15	14	12	10	11	10	15	24	16	14	14	16

Clinical Results.—The effect of the operation on each symptom is shown in the following diagrams. Symptoms (*Fig.* 73) were classed as:—

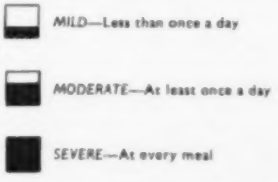

FIG. 73.—Key to symptom charts.

Dysphagia (*Fig.* 74).—Dysphagia was severe in all cases. Most claimed that fluids helped to wash the

solid foods down, but 5 had spells when they could not even swallow water. The operation cured the dysphagia in 7 cases. Eight patients still suffer; 1 severely, 3 moderately, and 4 mildly. The 7 patients with moderate or mild dysphagia all say that their swallowing is improved sufficiently to have made the operation worth while.

FIG. 74.—Dysphagia.

Regurgitation (*Fig.* 75).—Regurgitation was the second commonest symptom, but it was more variable in its severity. The operation cured 13, which makes this the most successful response of all. Acheson and Hadley (1958) point out that regurgitation is much more embarrassing socially than dysphagia and suggest that patients are often satisfied with the operation in spite of persistent dysphagia if their regurgitation is cured. This was true in this series, for the only patients who thought the operation not at all successful were the two with persistent regurgitation.

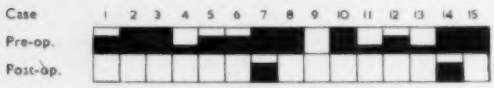

FIG. 75.—Regurgitation.

Dyspepsia (*Fig.* 76).—Five patients had dyspepsia before the operation; by dyspepsia we mean many vague post-prandial sensations such as fullness, flatulence, mild nausea, and epigastric discomfort. One is cured, the others are unchanged. More interesting is the development of dyspepsia in 7 cases since the operation; 1 severe, 1 moderate, and 5 mild, so that 11 cases out of 15 now have dyspepsia.

FIG. 76.—Dyspepsia.

Pain (*Fig.* 77).—This was not common. In each case it was retrosternal or high in the epigastrium and the patients described it as a severe heartburn. It always occurred within fifteen to thirty minutes of beginning a meal. The operation cured 2 of the 5 cases suffering in this way, 2 have been improved, and 1 made worse. We have not confirmed the findings of Douglas and Nicholson (1959), who found a high post-operative incidence of heartburn due to œsophageal reflux. The one case with reflux (*Case* 15) does not have heartburn.

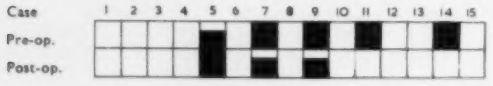

FIG. 77.—Pain.

Loss of Weight.—All patients lost weight in their pre-operative dysphagic period. The greatest loss was 3½ stone. Fourteen gained weight after operation and many said that they needed to restrict their diet to stop becoming overweight. The return to normal weight was rapid, frequently taking but a few months. The one patient who has lost weight since operation is surprisingly one of the good results.

Anæmia.—Wulff and Malm (1949) reported a high incidence of anæmia following cardioplasty. *Table II* shows that none of our patients on whom we have hæmoglobin estimations was or is anæmic.

Assessment of the Clinical Results.—We based our assessment of the clinical results (*Fig.* 78) upon the following criteria:—

Cure —No symptoms
Good —One or two mild symptoms
Moderate—More than two mild but less than three moderate symptoms
Poor —Three moderate or one severe symptom.

The psychoneurotic patient was made worse. The remainder claimed to be improved despite the persistence of symptoms. This is understandable when the severity of the original symptoms and their effect on the patient's social life is fully realized. However, the impressions of patients are not sufficiently objective and many who claim to be cured are, in fact, only improved. In this way the results resemble those of gastrectomy where the exchange of an unbearable symptom such as pain for a mild degree of 'dumping' seems like a cure. Similarly from intolerable dysphagia to dysphagia once a day or once a week is also a cure from the point of view of many patients. This may explain the high cure rates claimed in those series that do not present the long-term results in detail.

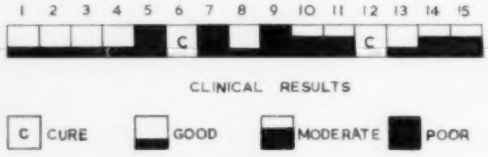

FIG. 78.—Clinical results.

The results are not good. The acceptable results are the 2 cures and the 6 good results. This leaves 7 unacceptable results out of 15 (47 per cent), 4 moderate and 3 poor.

Table II.—HÆMOGLOBIN CONCENTRATION

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Pre-operation	?	?	?	?	?	?	95	100	?	?	90	94	98	102	?
Post-operation	107	?	?	105	98	91	91	96	73	107	?	95	?	92	105

PART II. RADIOLOGICAL

Radiological Material (*Fig.*79).—Radiological examination of the œsophagus was carried out in 1959 on 13 cases. Four of these patients lived at some distance from this hospital and therefore attended their local hospitals for examination. Two patients (*Cases* 8, 11) refused further X-ray examination but 1 of these (*Case* 11) had a barium swallow in 1955 which was used for comparison with her pre-operative films.

FIG. 79.—Radiological material.

Eight of these 13 (*Cases* 5, 7–15) had pre-operative radiographs available for comparison with the new series.

In addition cinéradiographs were made of 6 patients.

It was not possible to measure the calibre and length of the œsophagus accurately as the films were taken on screening units and therefore subject to variations in magnification, but by comparing the two series of films in each case a rough estimate was made of any change in size of the œsophagus.

Radiological Results.—The radiological follow-up examination was intended to show:—

1. Whether the signs of achalasia were still present, i.e., (*a*) Obstruction at the lower end of the œsophagus; (*b*) Abnormal œsophageal movements; (*c*) Abnormal shape of the lower end of the œsophagus.

2. Whether there was evidence of any complications of the operation.

1. *Evidence of Persisting Achalasia.*—

a. Obstruction of the lower end of the œsophagus: At the 1959 examination 5 patients (those classified as 'cured' in *Fig.* 80) had no delay at the lower end of the œsophagus in the erect position, no food residue in the œsophagus, and no dilatation of the

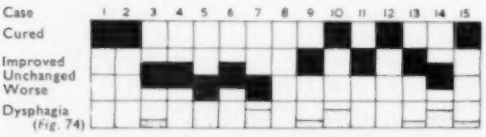

FIG. 80.—Comparison of clinical and radiological results.

œsophagus. Pre-operation films were available in 3 of these patients—in all these there had been delay, food residue, and dilatation.

Nine patients had persistent obstruction with delay, food residue, and œsophageal dilatation. Pre-operative films were available in 6 of these. In 3 patients ('improved', *Fig.* 80) the œsophagus had definitely decreased in size, suggesting that there had been partial relief of the obstruction. In 1 patient there was no definite change. In 2 patients ('worse', *Fig.* 80) the œsophagus had increased in size, indicating persistent obstruction.

b. Œsophageal movement: In the 8 cases of the 1959 follow-up examined personally no peristalsis was seen in the œsophagus. The absence of peristalsis was most obvious in the horizontal position in which the œsophagus appeared as a flaccid bag which filled with barium from the gastro-œsophageal junction to the pharynx as the patient continued to drink.

Three of these patients had no delay at the cardia in the erect position, but in the horizontal position the œsophagus failed to empty. In the erect position the normal 'stripping' wave of peristalsis which follows swallowing was absent in all cases.

Tertiary contractions were seen in every case in both the pre-operative and post-operative series of films. These are rapid local contractions of the circular muscle of the œsophagus which are seen in cases of œsophagitis, in achalasia, and in the elderly, but which are not seen normally in young adults. They were best seen in the concavity at the level of the aortic arch and just below the arch. They varied very much in number and in rapidity of formation and relaxation. In several patients they were more active in the horizontal than in the erect position. In the horizontal position active tertiary contractions caused to-and-fro movement of the barium within the œsophagus and tended to return the barium to the less active and more dilated part of the œsophagus above the aortic arch.

c. The shape of the lower end of the œsophagus: All the pre-operative films showed the cone-shaped lower end of the œsophagus and narrow segment which is considered typical of achalasia. In the follow-up series 4 cases remained this shape—all were considered poor results clinically and radiologically on other grounds. The lower end of the œsophagus appeared distorted with irregular mucosal folds in all the other post-operative films.

The maximum diameter of the narrow segment was measured on the film of each series in which it appeared widest. This diameter, not allowing for magnification, was 0·1–0·5 cm. pre-operatively and 0·1–1·0 cm. post-operatively. There was no close correlation between the width of the channel in the narrow segment and the presence of obstruction.

2. *Evidence of Complications of the Operation.*—A small hiatus hernia was present in *Case* 10, but no reflux could be produced at the time of the examination.

Gastro-œsophageal reflux was seen in 1 case (*Case* 15), in which reflux occurred in the supine position. There was no radiological evidence of œsophageal ulceration or stricture in any case. However, these are late signs of severe œsophagitis; mild œsophagitis cannot be diagnosed by radiological examination.

Assessment of Radiological Results.—The radiological assessment of the success of the operation was based upon the presence or absence of obstruction at the lower end of the œsophagus at the follow-up examination (*see Fig.* 80). (1) Five patients without obstruction were considered cured; (2) One patient was unchanged; (3) Three (*Cases* 3, 4, and 6) had persistent obstruction but no pre-operative films were available for comparison and therefore must be considered unchanged; (4) Two were worse.

Of the 5 patients classified as cured 1 had a small hiatus hernia without demonstrable reflux and 1 had free gastro-œsophageal reflux.

PART III. COMPARISON OF CLINICAL AND RADIOLOGICAL RESULTS

(*Fig.* 80)

There was some correlation between the radiological and clinical results in that the 8 cases with radiological improvement all had improvement of their dysphagia and regurgitation.

Four patients had good clinical improvement but radiological evidence of obstruction.

Thus, radiological improvement is a good indication of clinical improvement, but clinical improvement is not in itself an indication of relief of obstruction.

We had assessed the clinical and radiological results independently and were surprised by the degree of agreement in view of the accepted teaching that the clinical and radiological changes bear little relation to each other.

COMMENTS

It is well established that achalasia is a disorder of the whole œsophagus, although the most important symptoms and signs are due to obstruction caused by failure of relaxation of the lower end.

Heller's operation is designed to relieve the obstruction at the narrow segment but has no effect upon the functional abnormality of the body of the œsophagus. This is shown clearly in the 5 patients in whom the obstruction was completely relieved. In 4 of these cases the œsophagus below the aortic arch had returned to normal or less than normal calibre. Abnormal tertiary contractions persisted in all cases and no peristalsis was seen. It has been stated (Templeton, 1948) that tertiary contractions are more active in the relatively narrow than in the grossly dilated œsophagus. Observations in our series support this and also the statement that in treated cases of achalasia the silhouette of the œsophagus may resemble diffuse spasm (Olsen, Schlegel, Creamer, and Ellis, 1957).

Case 10 had no dysphagia for seven and a half years after his operation, that is, until early in 1959. Radiological examination three months after the recurrence of symptoms showed the œsophagus to be of narrow calibre with active tertiary contractions and no delay at the lower end. This appearance was reported at the time as 'diffuse spasm of the œsophagus'. The pre-operative films of this case showed the typical radiological appearance of achalasia and we consider this to be the correct diagnosis. The recurrence of dysphagia associated with very marked tertiary contractions and narrowing of the œsophagus below the aortic arch raises the possibility that this may be the usual appearance in the early stage of achalasia before persistent contraction at the cardia and œsophageal dilatation develops. We found at the follow-up examination that *Cases* 1 and 15 had very similar appearances.

Cinéradiography has a limited application in the study of achalasia. It has no advantage over the usual screening methods in the diagnosis of the condition or in the assessment of the degree of obstruction. The absence of peristalsis and the presence of tertiary contractions can be observed on screening, but for detailed analysis of the timing, position, and form of the contractions cinéradiography is invaluable, and it is the only method of recording the œsophageal movements for future comparison. With present apparatus using a 5-in. image intensifier there is the disadvantage that only a small segment of the œsophagus can be seen at any one time. In this series analysis of the cinéradiographs merely confirmed the impression obtained from screening of the extreme variability of these movements in different patients. It is probable that in the future further information regarding the natural history of achalasia will be obtained by follow-up cinéradiography of patients at regular intervals, three- or five-yearly, for example.

In 7 patients the œsophageal dilatation proved to be reversible when the obstruction at the lower end was relieved. *Case* 12 had a grossly enlarged œsophagus before operation; it was dilated and lengthened with the J-shaped lower third of severe achalasia, but the 1959 films showed only moderate dilatation in the horizontal position and in the erect position the calibre was within normal limits. It is commonly stated that Heller's operation, whilst producing a clinical cure, is unlikely to cause any recovery of the secondary enlargement of the œsophagus. This is not our experience. We consider that even the most grossly dilated and tortuous œsophagus can undergo considerable recovery if the obstruction is properly relieved.

Gastro-œsophageal reflux was seen in only 1 patient, but 3 others had symptoms (heartburn) suggestive of reflux and can therefore be presumed to have intermittent reflux through the cardia. This is hardly surprising following an operation that interferes with the sphincteric mechanisms of the cardia. What is remarkable is that 2 of these 3 patients with heartburn (*Cases* 5 and 7) have marked obstruction. One would think that a wide channel, without hold-up, would be required to allow an appreciable degree of reflux, unless, of course, this heartburn of which the patients complain is not due to reflux œsophagitis at all.

In our opinion too much stress has been laid on the importance of curing the symptoms and ignoring persisting obstruction seen on the radiographs. Ideally a cured patient should have a normal barium swallow and our efforts should be directed towards finding a method of treatment that achieves this. Heller's operation is a mechanical answer to a problem of function. It aims only to restore the ability of the œsophagus to act as a passive conducting tube between pharynx and stomach. It is not the solution to the problem of achalasia, for it cures but a few (15 per cent) and gives good clinical improvement in only half. The final answer to achalasia will solve the problem of the absent peristalsis and œsophageal spasm as well as ablating the obstruction at the cardia.

Nevertheless, Heller's operation is a useful method for treating achalasia. It rarely makes the patient worse, so that one can quite safely guarantee the patient some improvement, and so great is the disability of the disease that even this is gratefully accepted.

SUMMARY

1. Fifteen cases of achalasia, treated by Heller's operation between 1948 and 1956, have been reviewed.

2. Clinical and radiological results are presented separately and then correlated. Only 2 patients were cured, but 6 others had good results.

3. Comments have been made on the failure of Heller's operation as a curative procedure and on certain aspects of the post-operative changes in the œsophagus.

Acknowledgements.—We wish to express our thanks to Professor R. Milnes Walker and Dr. J. H. Middlemiss for their help and advice, to Mr. W. M. Capper, Mr. R. E. Horton, and Mr. J. H. Peacock for permission to follow-up their patients, and to Dr. F. G. M. Ross for the cinéradiography.

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SPONTANEOUS ATLANTO-AXIAL DISLOCATION

PATHOGENESIS AND TREATMENT WITH REPORT OF A NEW OPERATIVE PROCEDURE

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THE transverse fibrous band which passes across the back of the odontoid process is perhaps the most important ligament in the body since life depends on its integrity. If it is ruptured and flexion of the head occurs, the atlas can move forwards on the axis, the unrestrained odontoid approach the posterior arch of the atlas, and, the medulla being squeezed between them, death may be instantaneous. Examples of this have been known for a long time.

HISTORICAL

One of the earliest recorded cases of spontaneous atlanto-axial dislocation is that described in 1830 by Sir Charles Bell in a man with deep ulceration on the back of his throat, which produced destruction of the transverse ligament: "The atlas falling forward carried the spinal marrow against the tooth-like process and crushed it." John Hilton, in his classical lectures on "Rest and Pain" (Jacobson 1920), relates a case which he saw in 1841 of a child aged 5 years and 5 months regarding whom he had given strict orders that she be nursed lying flat in bed, with her head between sand-bags. He tells how the nurse ". . . this meddling and officious woman, instead of giving the child her breakfast as usual, without disturbing her head or neck in the least degree, desired the child to sit up to breakfast. The child did so: the head fell forward, and she was dead." Autopsy disclosed the dislocation which he had diagnosed and the fatal crushing of "the spinal marrow close to and below the medulla oblongata at the point of decussation, so that the child was killed almost instantly, as in pithing animals".

"A nurse was dressing sinuses in the neck of a girl aged 16, suffering from tuberculosis of the cervical glands with secondary pyogenic infection, and to better expose the area of the sinuses gently pushed the patient's cheek with the back of her hand as she asked her to turn her head. The child choked and died at once. Autopsy revealed that the transverse ligament had carried away and there was compression of the cord by dislocation of the atlas on the axis; 'the dens of the epistropheus had plunged into the medulla'." (Reid, quoted by Greig, 1931.)

CAUSES

As with spontaneous fractures of long bones, spontaneous dislocation at the atlanto-axial joint is the consequence of disease; in either case it may be precipitated by an injury so trivial that it would not occur in healthy tissues. The transverse ligament may be softened and stretched or partially or completely ruptured. Cases of spontaneous dislocation fall into two groups: those occurring most often in children and associated with inflammatory affections of the pharynx and nasopharynx (Desfosses, 1930; Grisel, 1930; Hess, Bronstein, and Abelson, 1935; Mabon and Lovell, 1956); and, less frequently, at later ages, e.g., Swanberg's (1919) case in a man aged 22 with acute tonsillitis, and others occurring later in life in association with the rheumatic diseases, particularly rheumatoid arthritis and ankylosing spondylitis (Boger, 1905; Kornblum, Clayton, and Nash, 1952; Coste, Auquier, and Civette, 1952; Vignon and Patet, 1955; Purser and Sharp, 1957; Séze, Dijan, and Caroit, 1957; Pratt, 1959), or tuberculous and other diseases of bone (Heaney and Whitaker, 1933). The dislocation, particularly when it occurs in children, is often eccentric and only partial, lateral displacement of the odontoid taking place in the atlas ring (Werne, 1955, 1957b) and accompanied with torticollis and stiffening of the neck muscles. In these cases there is fixation without any serious reduction of the lumen of the spinal canal. Movement of the atlas directly forwards is the most dangerous type of dislocation, being liable to produce medullary compression as the head is flexed.

The cases in children with acute throat infections have been called nasopharyngeal torticollis by the French writers, Desfosses and Grisel. X rays reveal forward dislocation with some rotation and slight lateral displacement of the atlas. This was at one

time ascribed to muscular spasm, but hyperæmia produced by the acute inflammation and decalcification of the atlas with loosening of the attachments of

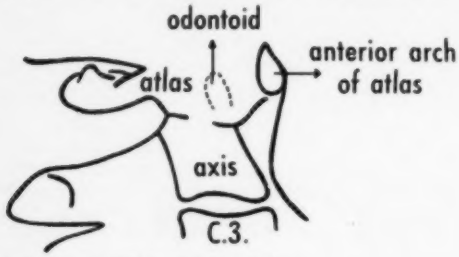

FIG. 81.—Atlanto-axial dislocation in a man aged 51 years with rheumatoid arthritis.
(Figs. 81, 82, by courtesy of The Department of X-rays and Illustration, Cardiff Royal Infirmary.)

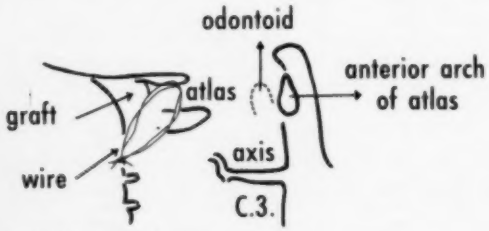

FIG. 82.—Same case after reduction of dislocation and fixation.

the transverse ligament, as suggested by Greig (1931) and supported by Watson-Jones (1932), is the more likely explanation.

Treatment of these cases in children is not difficult provided they are recognized early. All that is necessary is recumbency and rest with cervical extension by traction on the head and appropriate therapy for the inflammatory condition. Recalcification occurs with subsidence of the infection and resolution of the hyperæmia.

The problem of treatment is not as simple in adults with rheumatoid disease.

TREATMENT

Atlanto-axial Dislocation with Cord Compression.—When referring a patient with rheumatoid arthritis and dislocation at the atlanto-axial joint with signs of advancing compression of the spinal cord, a neurological colleague told me that he had twice seen such patients die suddenly from medullary compression. It was a matter of urgency, therefore, to prevent the atlas moving any further forwards on the axis, if possible after first reducing the dislocation. If this were not possible, excision of the posterior arch of the atlas with possibly the back of the foramen magnum and upper cervical laminectomy were indicated to relieve pressure on the cord by removing one side of the bony vice in which it was being compressed.

Reduction of the dislocation and fixation appeared to be the better alternative and could probably best be effected by exposing the under surface of the occiput and the upper part of the spinal column, bringing the advanced atlas back to its normal relationship with the axis, maintaining it in position with wires passed through its neural arch and the massive spinous process of the axis, and grafting the spines and the laminæ of the upper cervical vertebræ to the under surface of the occiput to bring about fusion.

CASE REPORT

A banker, aged 51 years, had suffered from severe rheumatoid arthritis since Christmas, 1955. In March 1959 he noticed tingling down both arms and down the left leg when flexion of the neck took place. This was followed by progressive weakness and stiffness, particularly of the left leg which had a tendency to jump, and by an inability to distinguish the nature of cloth or other material in his hand or to identify coins held in the palm of his hand. He had spastic tetraparesis with brisk tendon reflexes and bilateral extensor plantar responses. There was no definite sensory level but a change in acuity to pinprick at the level of the clavicles, or just below them. The protein in the lumbar cerebrospinal fluid was 180 mg. per 100 ml., with no increase in cellular content. X rays showed atlanto-axial dislocation and myelography a block at that level (*Fig.* 81). An operation for reduction of the dislocation and fusion as above planned was performed on Nov. 5, 1959, two stainless steel wires being passed between the dura mater and the posterior arch of the atlas and then through holes drilled in the massive spinous process of the axis. Bone chips for the fusion were obtained from the iliac crest. Plaster fixation was

maintained until April, 1960 (*Fig.* 82). Recovery was gratifying, the signs of pyramidal involvement disappeared. He remains well and able to walk normally, the atlas being in normal relationship to the axis, and he has returned to his work in the bank.

COMMENTS

I have been able to find published reports of only 4 other cases of spontaneous or non-traumatic atlanto-axial dislocation treated by operation; those of Rand (1944), Titrud, McKinlay, Camp, and Hannah (1949), and Margulies, Katz, and Rosenberg (1955) in the United States; and that of Pratt (1959) in this country. In the first three laminectomy was also performed to relieve pressure on the cord; in Pratt's case the dislocation was not reduced but a wire was placed between the external occipital protuberance and the axis to prevent flexion of the head, and bone-grafting was carried out.

In traumatic cases the odontoid is often fractured across its base allowing the atlas to move forwards just as if the transverse ligament had parted. When these traumatic cases have been operated upon laminectomy also has usually been the operation performed with, in some cases, removal of the back of the foramen magnum also (Pilcher, 1910; Kahn and Yglesias, 1935; and others). In 1910 Mixter and Osgood, in Boston, attempted to reduce the dislocation by pressure backwards through the pharynx on the anterior arch of the atlas while pulling on its posterior arch with a silk thread passed through it, but the dislocation having been present for six months, little impression was made upon it. The silk thread was then tied around the hooked spinous process of the axis. In the same year also, Ely, in New York, tied together with silk thread the posterior arches of the atlas and axis of a boy aged 16 years to prevent further dislocation occurring, but was unable to reduce the dislocation which, as in Mixter and Osgood's case, was old-standing, having occurred 8 months before. Provided the operation is not unduly delayed, however, there should be no difficulty in reducing the dislocation and carrying out the procedure I have described of wiring the posterior arch of the atlas to the spine of the axis and bone-grafting as a single-stage procedure, thereby avoiding laminectomy and opening the dura mater, and also a second operation for grafting at a later date.*

* Since reporting this procedure some French writers have recorded cases similarly treated. *Neuro-Chirurgie (Paris)*, (1960), **6**, 197.

SUMMARY

The pathogenesis and treatment of spontaneous atlanto-axial dislocation are discussed and a case is recorded in which tetraparesis complicating rheumatoid arthritis was treated by reduction of the dislocation without laminectomy, atlanto-axial wiring and fusion being carried out as a single operation. It is suggested that this is preferable to hitherto recorded two-stage procedures which, leaving the dislocation unreduced, involve laminectomy and, some months later, bone-grafting.

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MULTIPLE FIBROMATA OF THE TUNICA VAGINALIS

REVIEW OF THE LITERATURE AND CASE REPORT

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MULTIPLE fibromata of the tunica vaginalis testis is a rare condition. The first case recorded in the British literature is that of Sir George Makins (1912), who noted that previous references mentioned single fibromata rather than multiple tumours. Makins's case differed from previous cases, (*a*) in the multiple nature of the tumours, and (*b*) in the firmness of the structure of the fibromata.

Gordon-Taylor (1934) described a case in which there were three nodules for which he performed a 'blind' castration. He was also able to trace 13 recorded cases of fibromata of the tunica vaginalis.

More recently Labess (1950) reported a case in a 62-year-old man who had had a swelling in the right part of the scrotum for 25 years. Here the tumour consisted of a large number of irregularly shaped masses, which were confined within and projected from the walls of the tunica vaginalis. Histology showed a neoplastic process of the tunica vaginalis consisting of collagenous connective tissue.

FIG. 83.—Photograph of the lesion in situ. It can be seen that the nodules are distinct entities within the tunica vaginalis, which in this case is not thickened. From the macroscopical point of view the lesion appears to be a neoplasm rather than an inflammation.

The case described below is similar to those of Makins, Gordon-Taylor, and Labess.

More extensive reviews have been made by Goodwin (1946) and Hinman and Gibson (1924). Goodwin suggests that there may be two lesions: (1) Chronic proliferative periorchitis; (2) Multiple fibromata of the tunica vaginalis, the former being an inflammatory lesion and the latter a neoplastic process.

Anderson (1959) adheres to the view that the pathology is inflammatory in nature. He probably comes to this conclusion on account of the histological picture which often, but by no means always, shows evidence of inflammatory reaction (i.e., infiltration with lymphocytes and plasma cells).

On studying the literature it would appear that there are two further similar lesions: (1) Single benign fibroma of the tunica vaginalis. These are probably more common than multiple fibromata (Kocher, 1887; Thompson, 1936; Kawaichi, 1949). (2) Fibrosarcomata of the tunica vaginalis (Rubaschow, 1926; Trinidad and Sutton, 1953; McDonald, 1955).

CASE REPORT

HISTORY.—The patient was a clerk aged 39 years who, since the age of 34, had noticed some steadily growing nodules in the left part of his scrotum. Some two months previously they had grown more rapidly and had become somewhat painful. Nevertheless, the pain was not sufficiently severe to interfere with his work. There was no history of trauma. He was perfectly fit, was married, and had two normal children aged 8 and 14.

FIG. 84.—Photomicrograph showing the histology of one of the nodules on the tunica vaginalis. The section shows collagenous fibrous tissue with a whorled architecture. The tissue is infiltrated with lymphocytes and plasma cells. (× 80.)

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ON EXAMINATION: General examination: N.A.D. Scrotum: Right testis, epididymis, and vas deferens normal. Scattered throughout the left half of the scrotum there were several nodules varying from ¼ in. to ¾ in. in diameter. Although the left testis and epididymis were palpable, it was difficult to decide whether they were involved in the process.

It was decided to explore the scrotum.

OPERATION AND FINDINGS.—Exploration of the scrotum under general anæsthesia through a left scrotal incision.

Findings (*Fig.* 83): L. vas deferens and vessels were normal. The tunica vaginalis had scattered throughout its substance eight nodules, most of which had diameters varying from ¼ in. to ¾ in. There were two further nodules of similar size which appeared to involve both the epididymis and the testis where these are in apposition.

After discussion it was decided that epididymo-orchidectomy and excision of all the nodules should be performed. This decision was not lightly undertaken, but it was felt that the history of recent rapid growth must be taken into account. It was also thought that biopsy of a possibly malignant tumour within the walls of the scrotum was not justified.

HISTOLOGY (*Fig.* 84).—Sections of one of the multiple circumscribed nodules scattered throughout the tunica vaginalis show collagenous fibrous tissue which has a whorled architecture. The tissue is infiltrated with numerous inflammatory cells (lymphocytes and plasma cells).

The slides were shown to a number of pathologists. From their reports it would appear that there is no unanimity as to the diagnosis: some believe that the lesion is neoplastic in nature, i.e., a fibroma; others have come to the conclusion that the lesion is basically inflammatory. Five members of the testicular tumour panel and registry have so far given their opinion, and two other pathologists, not members of the panel, have reported on the sections.

An analysis of their reports appears as follows: Chronic inflammation, 2; Fibroma, 3; "Fibroma", 1; "Fibromata" (? post inflammatory lesion), 1.

SUMMARY AND CONCLUSIONS

A case of multiple fibromata of the tunica vaginalis is presented with a review of the literature. Pre-operative diagnosis is not possible. The scrotum should be explored.

If the history suggests that there has been no recent activity of the lesion then a conservative course of action is justifiable (i.e., biopsy followed by excision of the nodules). A proportion of surgeons reporting this condition have resorted to immediate 'blind' castration.

Macroscopically the lesion appears to be a neoplasm, but microscopical examination throws doubt on this view on account of the presence of many inflammatory cells.

Acknowledgements.—My grateful thanks are extended to Mr. R. Lawrie, under whose care the above patient was admitted and whose advice enabled me to write this paper. Additional thanks are due to Dr. R. S. Ralph and the members of the testicular tumour panel for their reports on the pathology.

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PNEUMATOSIS CYSTOIDES INTESTINALIS INVOLVING THE LEFT HALF OF THE COLON AND RECTUM

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PNEUMATOSIS cystoides intestinalis is a rare condition characterized by subserous and submucous collections of gas and most commonly affects the small intestine.

An increasing number of papers has appeared in recent years in which the condition has been confined to the colon, and has been diagnosed on sigmoidoscopy. In an excellent paper from the Mayo Clinic, Smith, Anderson, and Pemberton (1958) found 27 cases in the world literature in which only the left colon was involved, and added 4 cases of their own. Other cases have been added since then by Creevey, Cohen, and Riley (1958), Littman (1958), Marion (1958), the case reports of the Massachusetts General Hospital (1958), Mujahed and Evans (1958), Nelson (1958), and Calne (1959).

Involvement of the rectum is extremely rare and has been reported in 4 other cases: Griffiths (1955), Kohler and Wurm (1955), Ramos and Powers (1957), and Shoesmith and Crone (1959).

A further patient in whom the left half of the colon and rectum were involved is described.

CASE REPORT

Mrs. B., 49 years, housewife, was first seen in the Out-patient Department on March 3, 1960. Over the past year her bowels had been opened only every third day, but she passed at frequent intervals large quantities of mucus streaked with blood. The blood was never mixed with the motion and there was no history of diarrhœa. She had had a hysterectomy and an appendicectomy 12 years and 8 years ago respectively. Unfortunately no operation notes were now available, but her family doctor had no record that the bowel was found to be abnormal at these times. A leucotomy had been performed 4 years previously and she was still taking large doses of barbiturates.

ON EXAMINATION.—She was a well-built lady and apart from the laparotomy scars no abnormality was found in the abdomen. On the anterior wall of the rectum there was a firm, elastic, sessile lesion about 5 cm. across, with a further smaller polypoidal lesion alongside. The

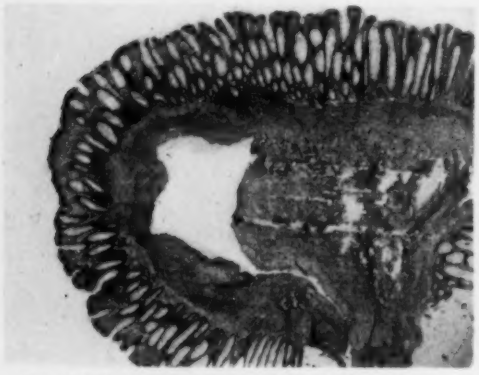

FIG. 85.—Showing rectal mucosa and cystic space (× 16·5.)

mucosa felt quite intact over these lesions. No blood was seen on the glove, but it was smeared with mucus. The nature of the lesion was not realized on proctoscopy, but it was noted that there were some semitranslucent areas, and that the mucosa was intact. It was thought not to be a carcinoma and a biopsy was taken.

Pathology (Dr. J. L. Edwards).—

"From: Rectum.

"*Macroscopically*: Three nodules each 0·5 cm. diameter; one of the nodules floated.

"*Microscopically*: Giant cells are abundant and appear to be related to cystic spaces. These complexes are in the fibrous tissue immediately deep to epithelium." (*Figs.* 85, 86.)

On discussion it was thought that the cystic spaces contained either a fatty substance or gas. That the lesion might have arisen following an injection for hæmorrhoids was considered, but was ruled out by its position and a negative history.

A further biopsy was obviously necessary and this was taken through the operating sigmoidoscope. An excellent view was obtained and the lesion was seen to be made up

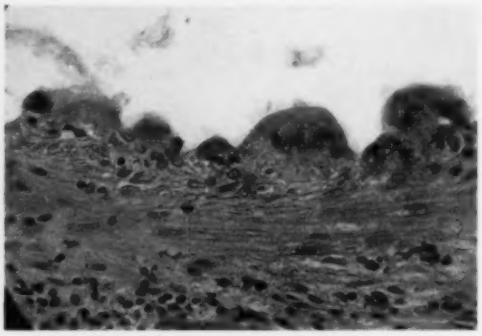

FIG. 86.—Giant cells lining the cystic space. (× 292·5.)

of many semitranslucent cystic areas, varying in size from minute to 1 cm., and covered with normal mucosa. These cystic areas started at 8 cm. from the anal margin, and were seen to project into the lumen of the bowel as far as 26 cm.

Pathology (Dr. J. L. Edwards).—

"From: Rectum.

"*Macroscopically*: Three fragments received each approximately 0·6 cm.^{3}. Two were taken by diathermy—of these one sank in saline (labelled 1); the second floated in saline (labelled 2); the third fragment floated in saline (labelled 3). Each of the fragments was bisected under saline and several obvious bubbles of gas came to the surface from specimen 3, and, to a lesser extent, from the

FIG. 87.—Barium enema at the stage of rectal filling, showing numerous small cysts and one large one at the recto-sigmoid junction.

FIG. 88.—Barium enema showing numerous small and large cysts indenting the contour of the sigmoid and descending colon.

other floating specimen (2). The floating specimens (2 and 3) then sank.

"*Microscopically: Specimen* 3. About half the submucous tissue consists of a space lined by giant cells of foreign-body type with evidence of local chronic inflammation. The appearances are deemed consistent with the so-called 'pneumatosis intestinalis'.

"The other two specimens are not so satisfactory, but are deemed consistent with the same condition. I see no indication of neoplasm in any of this material. The fact that when dissected under saline gas, and not oil, emerged from this material amounts to virtual proof of the diagnosis. The cavities show no evidence of fat."

Radiographic examination was performed by Dr. T. Lodge to determine the extent of the lesion. He reported: "*Abdomen*: Large gas-distended rectum and excess of gas in the distal colon which in addition to intraluminal gas shows a generalized honeycomb pattern due to multiple, small, round gas shadows. *Conclusions*: Pneumatosis cystoides intestinalis.

"*Barium Enema.*—This showed numerous small semicircular filling defects at the edges of the sigmoid and the distal colon generally. At one point in the sigmoid two of these large defects on either side simulate an annular carcinoma. *Conclusions*: The appearances are consistent with gas cysts due to pneumatosis intestinalis. (*Figs.* 87, 88.)

"*Barium Meal and Follow-through Examination.*—This showed a small hiatus hernia, but no cysts were demonstrated in the small bowel or in the large bowel as far as the mid-transverse colon."

DISCUSSION

The majority of cases of pneumatosis affecting the left colon have been described since 1947. Smith, Anderson, and Pemberton (1958), in their review, could find no reason for this apparent increase, the only common factors being an age incidence of over 45 years, debility, and a preceding enteritis.

The aetiology of the condition remains obscure and the theories of its causation—mechanical, neoplastic, bacterial, and dietary deficiency—have been reviewed by Alford, Galletti, and Culver (1956).

Cases have been reported in which the condition developed following operation on the colon, either sigmoidoscopy (Marshak, Blum, and Eliasoph, 1956; Kreeger and Littman, 1954) or resection (Sedgwick and Ruddell, 1954; Marion, 1958), but it is an extremely rare complication.

When the condition affects the left colon, it is usually limited to this region, and associated gastrointestinal lesions are rare; this contrasts with small-bowel involvement when stenotic duodenal ulceration was found in 55 per cent of cases (Koss, 1952).

The sexes are equally affected, there being 20 females and 22 males in the cases so far recorded, including the case presented here.

The symptoms were very similar to those of other large-bowel lesions and were no help in the diagnosis. The passage of blood and mucus per rectum were very common symptoms, the bleeding apparently coming from congested mucosa overlying the cysts, although this was not demonstrated in the present case. Episodes of abdominal pain due to sub-acute obstruction were also quite frequent.

On sigmoidoscopy the lesions have been mistaken for multiple polyposis or carcinoma.

If the cysts are large enough they may deflate on attempted biopsy and the diagnosis has been reached in this way on several occasions.

Although the segments of colon containing cysts have been opened under water and thus shown to contain gas, I have found no reference to this being done on the small biopsy fragments.

It was perhaps fortunate that in the present case the gas cysts were so small that they remained intact in the biopsy fragments, but nevertheless the demonstration of gas bubbles coming from the cut surface was easily seen.

Radiologically these lesions have been mistaken for multiple polyposis, polypoid change in ulcerative colitis, or carcinoma, but as the condition becomes more widely recognized further cases should be diagnosed sigmoidoscopically and radiologically.

Obstruction, hæmorrhage, volvulus, and pneumoperitoneum may complicate the condition, which is essentially a benign one and surgical treatment should be reserved for these complications. Indeed the cysts may disappear spontaneously. If the symptoms are severe enough and the condition is localized to the lower sigmoid, it may be worth attempting to deflate the cysts through the sigmoidoscope.

SUMMARY

A case is described of pneumatosis cystoides intestinalis involving the left side of the colon and rectum in a 49-year-old woman. Her symptoms were those of constipation and the passage of mucus and blood per rectum.

The cysts were seen on sigmoidoscopy.

Conservative treatment is being followed.

Acknowledgements.—I wish to thank Dr. Wilkes, of Baslow, for referring the patient; Mr. D. J. Robertson for permission to investigate and present this case; Dr. J. L. Edwards for the pathological reports and his considerable help in the diagnosis; Dr. T. Lodge for the barium studies; Mr. J. F. V. Larway and Mr. Cousins for the photographs.

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EXPERIENCES WITH DIFFERENTIAL RENAL FUNCTION STUDIES IN THE INVESTIGATION OF HYPERTENSION OF RENAL ORIGIN

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It is well known that certain cases of hypertension are due to renal abnormality, and that some of these cases may be cured, or at least improved, by surgical means. The main difficulty, however, lies in the selection of such cases, since the demonstration by routine methods of a renal lesion does not mean that its correction will necessarily influence the course of the hypertensive disease.

In recent years two new lines of approach to diagnosis in these cases have been suggested: namely the use of differential renal function studies by Connor, Berthrong, Thomas, and Howard (1957), and the radio-active diodrast excretion renogram by Winter (1957).

By 'differential renal function studies' is meant the synchronous collection of urine specimens from the two kidneys, under standard conditions, so that a comparative study may be made of certain of their physical and chemical components.

It is the purpose of this paper to attempt to evaluate these studies, in the light of present experience, as an aid to the selection of those cases of renal hypertension in which surgery, conservative or ablative, may be of use.

The study presented here was carried out over a period of eight months at the University of Michigan Medical Center, where the author worked in close liaison between the Section of Urology under Professor Reed M. Nesbit, in the Department of Surgery, and the Hypertension Research Unit under Professor Sibley W. Hoobler, in the Department of Medicine.

All patients referred to this hospital with hypertension are carefully evaluated by the Hypertension Research Unit in order first to establish those of known aetiology, such as phæochromocytoma, coarctation of the aorta, Cushing's syndrome, and primary aldosteronism. Those with essential hypertension, and any who were suspected of having a renal origin for their hypertension, were then reviewed, together with their excretory pyelograms, diodrast renograms, and other relevant data at a joint conference between the two Units. This conference decided which of these patients should be selected for further study by differential renal function tests and aortography.

During the period under review 558 patients were investigated by the Hypertension Unit, and of these, 30 were selected for differential function studies. The selection was as critical as possible, and no patient was subjected to these tests who was not considered fully fit to undergo such surgery as might be required to give him a reasonable chance of improvement of his hypertension. It should be emphasized, too, that these 558 represented all patients referred to the Unit, and that many were cases of labile hypertension or of such mild degree as not to require treatment.

Finally, all of these studies were carried out by the same person (the author) in order to ensure a uniform technique, and it was the aim of all who collaborated in this continuing study to try to assess the value of this test in terms of practical clinical usefulness.

RENAL HYPERTENSION

A variety of lesions affecting the kidney may be associated with hypertension. They include acute and chronic glomerulonephritis, polycystic kidneys, occlusive renal vascular disease, chronic pyelonephritis, and possibly hypoplasia. Occasionally hydronephrosis, tuberculosis, and lower urinary tract obstruction are similarly associated, but in these the hypertension is often of secondary importance. Glomerulonephritis and polycystic disease, being bilateral conditions, are not usually amenable to surgery. On the other hand, hypertension associated with occlusive renal vascular disease, and chronic pyelonephritis, both of which may be wholly or predominantly unilateral, is sometimes surgically remediable, and is therefore the principal concern of this investigation.

Occlusive renal vascular disease is most commonly due to atheroma, in which a localized plaque may be responsible, and which may occur in the fourth or even third decades of life. It also includes a type of stenosis described by Poutasse, Humphries, McCormack, and Corcoran (1956) as "fibrous intimal proliferation". This is seen mainly in children and adolescents, may be bilateral, and is probably developmental in origin. Other less common causes are aneurysm, thrombosis, embolism, and occasionally compression of the artery from without by a renal or extra-renal tumour. Multiple renal arteries also occur but, unless associated with any of the lesions just referred to, are probably not significant.

It seems likely that these various vascular lesions, by producing ischæmia and local hypotension, provide a human parallel to the classical experiments of Goldblatt, Lynch, Hanzel, and Summerville (1934) in the dog; though, unlike the effect on this animal, hypertension in the human is sustained rather than transient.

Whether chronic pyelonephritis causes hypertension in a similar manner, by the development of multiple minute areas of ischæmia, or involves some other and different mechanism, remains obscure.

EXPERIMENTAL BASIS OF DIFFERENTIAL RENAL FUNCTION STUDIES

In 1950 White reported the results of his experiments in dogs prepared by explanting the bladder trigone so that urine specimens could be collected separately and simultaneously from the two kidneys. He showed that by placing a ligature on one renal artery so as to restrict the blood-flow slightly, there was a reduction in the volume and sodium concentration in the urine from the kidney, with a corresponding increase on the unaffected side which thus maintained electrolyte balance. He explained this phenomenon by pointing out that the affected kidney

continued to reabsorb at much the same rate as before, in the presence of a reduced volume of glomerular filtrate, because the composition of the blood reaching it had not altered, since the normal kidney was preventing any accumulation from occurring. White further showed that this unilateral reduction in blood-flow could be great enough to produce a 50 per cent fall in volume and sodium concentration before inulin and para-aminohippurate clearances were measurably altered. So long as the normal kidney remained intact this state of affairs persisted, but if the normal kidney was removed, the other one, to which the artery remained constricted, then responded by excreting all the salt and water previously excreted by both kidneys.

In 1957 Connor and others published their experiences with hypertension of unilateral renal origin. By correlating White's experimental findings with the earlier work of Goldblatt and others (1934), they suggested that this decrease in urine volume and sodium concentration resulting from a reduction in blood-flow to one kidney might form the basis of a test helpful in the diagnosis of unilateral renal hypertension. (This test is sometimes referred to as 'the Howard test' and the work is subsequently referred to under this name.) In a review of 8 patients who underwent nephrectomy for hypertension, Howard and others reported that the test was consistently positive in the 4 who in fact had relief of their hypertension. These 4 had shown a reduced urine volume and sodium concentration on the affected side, while the other 4, whose hypertension was not relieved, had shown no such consistent changes. In the successful cases the volumes on the affected side varied from 41 per cent to only 9 per cent, and the sodium concentrations from 85 per cent to 63 per cent, of the respective values for the normal side. The final diagnosis in these 4 patients appears to have been renal vascular insufficiency in 3, and chronic pyelonephritis in 1.

Other experimental work which may have a bearing on differential function studies, and though not used by Howard and others has been included in similar studies by Schlegel, Savlov, and Gabor (1959), is that of Berliner and Davidson (1957), who also carried out certain renal vascular experiments in dogs. They applied an inflatable cuff, in which the pressure could be controlled from without through a polythene tube, to one renal artery. They found, on inflation of the cuff, and consequent diminution in the blood-flow to the kidney, that every measurable depression of the glomerular filtration rate was accompanied by a rise in the total osmotic concentration of the urine produced by that kidney; and this in spite of the fact that sodium and chloride concentrations were almost always lower in the urine from the experimental than the control kidney. This last observation adds further confirmation to the earlier observations of White. A comparison of the osmolalities may therefore be significant in differential function studies. (The term 'osmolality' is defined by Moore (1959) as osmolar concentration per unit total water, and is used throughout as such.)

TECHNIQUE

The method used for obtaining synchronous bilateral urine samples in the present investigation was based on that of Howard and others (1957) but differed in some minor details. It should be noted, however, that other investigators have used somewhat different techniques, and this might be responsible for variations in reported results. It has been borne in mind throughout that these studies, if they are to be of practical use in the hands of the average surgeon, and not become unduly tedious to the patient, must be kept as simple and short as is compatible with reliability. The values measured for comparison in this study included volume, sodium concentration, osmolality, and 15-minute phenolsulphonephthalein excretion (PSP). The technical details were as follows:—

1. Diet and Drugs.—Low sodium diets were discontinued as was chlorothiazide medication, at least five days prior to the test. These precautions may not be essential in a comparative study, but it was felt best to take them.

2. Anæsthesia.—Following barbiturate premedication, males usually received a general anæsthetic (thiamylal sodium, nitrous oxide, and oxygen), females a local one (2 per cent xylocaine jelly). It is now realized that this latter preparation contained a small amount of sodium carboxymethylcellulose, and a simple test showed that 50 ml. of distilled water to which had been added 1 ml. of the jelly contained approximately 2·3 mEq. l. sodium. Where sodium concentrations in the urine specimens are reasonably high, this will have had little effect on the results, but it illustrates the careful attention to detail which is necessary.

3. Hydration.—Oral or intravenous hydration was used, but the latter was preferred, even with local anæsthesia, since some patients felt nauseated by the amount of fluid they were required to drink (approximately 200 ml. per fifteen minutes, for one hour before and during the procedure), and this nausea was nearly always reflected in transient renal shut-down. Intravenous hydration is also preferable in that, with a little experience, it is easier to control the rate of total urine flow, the optimum flow being 1·5–3·0 ml. per minute. At lower rates collection becomes unduly tedious, while higher rates are apt to lead to leakage around the catheter into the bladder, which, if great enough, invalidates the test. Intravenous hydration consisted of 10 per cent dextrose in water, and it was found best to administer about 350 ml. in the thirty minutes prior to collecting, and the remainder of the litre during the actual procedure, the total time for which was usually about ninety minutes.

4. Cystoscopy.—This was carried out in the usual manner, No. 6 or 7 Charrière woven nylon whistle-tip ureteric catheters being introduced. No. 7 was preferred so long as it passed easily, but the same size was always used on both sides. Polyethylene catheters were also tried, but did not seem to pass so easily size for size. While the effect on the kidney of minor ureteric trauma is not known, it is at least advantageous to avoid contamination with blood. The catheters were passed to lie, so far as could be judged, just within the renal pelvis, careful reference having been made to the position of the kidneys on previous pyelograms. The cystoscope was then removed and a No. 16 Foley catheter introduced into the bladder, which was carefully emptied.

Table I.—Results of Differential Renal Function Studies

Patient	Volume ml.			Sodium Concentration mEq./l.			Osmolality mOsm./l.			15 min. PSP Per Cent		
	Rt.	Lt.	Bladder	Rt.	Lt.	Bladder	Rt.	Lt.	Bladder	Rt.	Lt.	Bladder
1	15 43	11 58	} 50	165 52	150 53							
2	33 51	32 47	0 0	57 31	60 32							
3	13	14	23	70	76	71						
4	42 24	38 22	0 0	25 90	21 85					5	10	?
5	37 47	53 62	0 0	50 37	58 43		466 372	413 342		7·5	10	0
6	10 10	12 28	5 1	82 79	101 98	109	232	559		2·5	37·5	0
7	12 46	15 39	0 37	238 36	98 25	47	134	93		17·5	7·5	7·5
8	16 9	52 36	0 7	43 39	38 31	30	496	522		7·5	25	0
9	62 57	24 24	5 1	12 27	12 23		611	321		25	7·5	0
10	49 43 37 41 22	4 2 4 5 3	42 35 24 41 18	100 106 16 70 76	87 42 34 58 70	95 92 40 74 76	386 382	352	375 372	10	0	7·5
11	11 18	18 26	0 0	40 17	45 17		697	627		15	27·5	0
12	14 14	13 12	0 0	34 25	35 29		672 772	720 829		15	15	0
13	133 122	7 6	12 13	2 2	5 6	6 5	60	56		7·5	0	2·5
14	32 11	60 33	30 25	10 6	8 6	17 8	160	160		5	25	20
15	38 44	19 26	23 56	42 15	41 14	41 16	393	406				
16	40	34	16	128	95	128	260	433				
17	35 65	1 2	3 3	48 28	21 25	42 32	222	285	210	22·5	0	10
18	38 26	10 5	5 7	57 69	50 56	35 57	530	496		22·5	2·5	2·5
19	50	49	0	10	7		592	652		10	20	0
20	14 14	13 14	0 0	56 59	36 37		264	236		7·5	5	0
21	70 76	74 77	13 19	14 13	15 14	27 24				12·5	7·5	17·5
22	13 14	13 15	0 0	94 76	97 80		517	516		15	20	0
23	17 24	14 26	0 0	19 20	18 18		543	470		10	7·5	0
24	16 14	8 12	6 4	18 19	17 19	27 30	686	675		10	7·5	0
25	14 15	11 14	0 0	16 14	9 15		791 244	703 261		15	10	0
26	19 10	9 11	? 0	15 17	17 17		630 579	661 492		7·5	12·5	0
27	23 29	26 33	0 0	67 66	67 67		389	294		12·5	15	0
28	22 14	40 25	19 5	19 13	20 15	24 19	167	226	192	5	17·5	5
29	41 23	23 8	47 51	85 42	84 44	88 40	409	394	401	10	15	15
30	62 56	14 13	0 0	12 5	25 11		146	159		22·5	7·5	0

5. Collection.—A few minutes were allowed to elapse until it was seen that there was a regular flow from each side. If the flow was suggestive of peristaltic activity it was assumed that the catheter lay below the renal pelvis, but this did not appear necessarily to predispose to leakage around the catheter. Two successive synchronous collections were then made for periods of fifteen to thirty minutes, the bladder being carefully emptied at the end of each collection. These specimens were used for volume and sodium concentration estimations. A third collection was then made for osmolality determination, using the Fiske osmometer, which employs a freezing-point technique. Finally, 1 ml. of PSP was given intravenously, and a further fifteen-minute collection made from each side, and if necessary from the bladder.

6. Estimations.—The reason for the two collections for volume and sodium concentration determinations was to act as a check on each other under, usually, differing rates of urine flow.

In the final results (*Table II*) the aggregate volumes are compared, together with the average sodium concentrations and osmolalities. When blood was present, giving a hæmatocrit reading of more than 1 per cent, which was unusual, the specimen was either discarded, or correction made for the amount of sodium present in the appropriate volume of whole blood, as described by Howard and others. The osmolality specimens were taken in centrifuge tubes, so that any cells present could be immediately spun out, and the samples frozen pending osmolality determination, to obviate alterations caused by bacterial action. The PSP collections could be used to provide a further check on comparative volumes, though it was not infrequently found at this stage of the procedure that leakage around the catheters into the bladder had become marked.

Table II.—A Correlation of Diagnostic Methods in Hypertension of Probable Renal Origin

1	2	3	4	5	6	7	8	9	10	11	12	13	
								Differential Renal Function Studies					
Patient	Age	Sex	Blood-pressure	Clinical Diagnosis of Hypertension	I.V. and/or Retrograde Pyelography	Aortography	Radioactive Diodrast Renography	Side of Lower Volume	Volumes per cent	Na Concentration per cent	Osmolality per cent	15 min. PSP per cent	
												R	L
2	40	F	105/60	Normotensive	N			L	94	104			
4	35	M	170/120	Essential hypertension	(L)		L	L	91	89			
5	55	M	200/135	Essential hypertension	N	N	RL	R	73	86	111	7·5	10
6	44	F	150/100	Hydronephrosis and chronic pyelonephritis	R		R	R	65*	82	42	2·5	37·5
8	36	F	160/110	Chronic pyelonephritis	R		R	R	36*	119	95	7·5	25
9	53	M	150/100	Chronic pyelonephritis	L		L	L	45*	93	53	25	7·5
10	60	M	200/100	Essential hypertension	(L)		(RL)	L	93*	107	92	10	7·5*
11	25	M	205/135	Essential hypertension	(R)	N	R	R	66	94	111	15	27·5
12	23	M	200/110	Essential hypertension	N	N	(R)	L	89	110	107	15	15
13	49	F	200/120	Chronic pyelonephritis	L	L	L	L	15*	275†	93	7·5	2·5*
17	55	F	205/120	Renal vascular occlusion	L	L	(L)	L	9*	66	128	22·5	10*
18	51	F	175/105	Chronic pyelonephritis	(RL)		L	L	42*	84	90	22·5	5*
19	62	F	170/110	Essential hypertension	N		L	L	98	70†	111	10	20
20	28	M	230/150	Chronic glomerulonephritis	N		R	L	96	64	89	7·5	5
22	34	F	230/140	Chronic pyelonephritis	R		N	R	96	96	100	15	20
23	54	M	240/140	Essential hypertension	N		(L)	L	98	92	87	10	7·5
25	39	M	170/120	Essential hypertension	(L)	Intramural injection	(L)	L	86	82	98	15	10

Columns 6–8 indicate that the kidneys were considered either normal, or that an abnormality was present on one or both sides which might be associated with the hypertension. N = Normal. R = Right. L = Left. Where letters are shown in brackets, an abnormality was present, but it was probably not so associated.

In columns 10–12 the values obtained on the side of lower volume are expressed as a percentage of the corresponding values on the side of higher volume. Column 13 shows the actual PSP values (to the nearest 2·5 per cent) obtained from the two sides.

* These figures may well be lower (but not higher), since for purposes of these calculations it was thought best to include any leakage into the bladder around the ureteric catheters as if it had come from the side of lower volume. (*See Table I.*)

† With very low sodium concentrations (i.e., below 10 mEq./l.) these figures are liable to be inaccurate. (*See Table I.*)

7. Precautions.—Two points should perhaps be emphasized. The first is that all apparatus, including cystoscopes, catheters, and collecting vessels, must be carefully washed out with sterile distilled water prior to use. The second is that the check for bladder urine due to leakage around the catheters must be a very careful one.

The complications of the procedure are, of course, those of any cystoscopy with bilateral catheterization, and include the possible introduction of infection, but perhaps it is worth recording that one of our patients (*Case* 27) became anuric for a period of forty-eight hours before resuming normal renal function.

RESULTS

In this investigation, 30 hypertensive patients underwent differential renal function studies. They had been selected, after careful routine evaluation, as possibly having a renal origin for their hypertension. In other words non-renal causes had been excluded as far as possible, leaving a group which is commonly labelled 'essential hypertension', but in which cases of chronic pyelonephritis and others with renal

arterial lesions may easily be overlooked. Microscopic and bacteriological studies on the urine, excretory pyelography, and radio-active diodrast renography had been done in all cases. Aortography was not routine, being done only in those cases which fulfilled the following criteria: (1) If the hypertension was considered to be of such severity as to constitute a definite threat to the patient's life. (2) Provided that the patient was considered fit to undergo such major renal or renal vascular surgery as the aortography might indicate to be necessary.

Table I shows the actual figures obtained in these studies. In most cases the two sets of synchronous specimens were obtained at the same session, though in one case (*Case* 10) the test was repeated at a later date. The bladder volumes show that in approximately one-third of these studies kidney volume comparisons were invalidated by excessive leakage around one or both catheters. Increasing experience did not seem to eliminate this difficulty, which constituted the commonest cause of failure in this test.

Table II shows the diagnosis made in 17 of the 19 cases with valid differential function tests, and attempts to correlate the results of these tests with pyelography, aortography, and radio-active diodrast renography. Under each of these headings is indicated the side on which a significant abnormality was noted. For instance an intravenous pyelogram might reveal

Table III.—Details of Studies in Cases with Diagnoses proved Pathologically

Patient	Age	Sex	Pre-operative B.P.	I.V. and/or Retrograde Pyelography	Aortography	Radio-active Diodrast Renography	Differential Renal Function Studies						Operation etc.	Pathology	Post-operative B.P.
							Side of Lower Volumes	Volume per cent	Sodium Concentration per cent	Osmolality per cent	15 min. PSP per cent				
											R.	*L.*			
6	44	F.	150/100	Gross R. hydronephrosis with two ureteric calculi. L., normal	Not done	Impaired blood-supply and function on R.	R.	65*	72	42	2·5	37·5	R. nephroureterectomy	Hydronephrosis and chronic pyelonephritis	140/90 (6 mth.)
10	60	M.	200/100	Poor visualization in I.V.P. bilaterally. L. kidney probably smaller than R. Retrograde normal	Not done	Probable bilateral impairment of function, L. slightly more so than R.	L.	93*	107	92	10	7·5*	(Died in acute heart failure while undergoing investigation)	Generalized arteriosclerosis. No evidence of renal vascular lesion, or past or present renal inflammatory disease. 'Essential hypertension'	
13	49	F.	200/120	Dye present bilaterally at 5 min., but L. < R. L. kidney 2 cm. shorter than R.	Normal R. vascular pattern. Poor visualization vessels on L.	Impaired blood-supply on L. with excretory delay on R.	L.	15*	275†	93	7·5	2·5*	L. nephrectomy	Chronic pyelonephritis with arterial and arteriolar nephrosclerosis	180/100 (4 mth.)
17	55	F.	205/120	Dye present bilaterally at 5 min., but L. < R. L. kidney 3 cm. shorter than R. Retrograde normal	Bilateral renal arterial obstruction, L. almost complete, R. minimal. Arteriosclerotic aortic changes	Probable impairment of function on L., but no definite evidence of impaired blood-supply	L.	9*	66	128	22·5	10*	Attempted L. splenorenal arterial anastomosis, failed owing to state of splenic artery. L. nephrectomy	Arteriosclerotic occlusive disease of L. renal artery. Evidence of old pyelonephritis	190/100 (2 mth.)

Differential function study values are expressed as in *Table II*.

* and †, as in *Table II*.

one kidney to be measurably smaller than the other, 1 cm. or more in length being considered as abnormal; there might be delay in excretion on one side; or the calyceal pattern might be suggestive of chronic inflammatory changes. In the renograms only gross evidence of impairment of function, on one side as compared with the other, was taken as significant, lesser changes being regarded as of doubtful importance; while in the aortograms the side indicated had been shown to have a definite impairment of its vascular supply. On this basis the table would appear to show good overall correlation between the various investigations, in that pyelography, aortography, renography, and the side of lower volume and PSP excretion all agree with reasonable consistency.

In this series of cases pathological proof of the renal status was obtainable in 4 cases, 3 by nephrectomy and 1 at autopsy. Two of these patients had unilateral, or predominantly unilateral, chronic pyelonephritis, 1 having a hydronephrosis and ureteric calculi on the affected side as well. One patient had arteriosclerotic renal vascular occlusion with evidence of old pyelonephritis. Finally, 1 had true essential hypertension. Particulars of these cases are shown in greater detail in *Table III*.

DISCUSSION

The study of differential renal function as an aid to the diagnosis of remediable renal hypertension has been stimulated by the work of Howard and others (1957). Since their original report this group has had further experience with the test, as reported by Scott (1959). Out of 20 hypertensive patients with positive tests, 19 have undergone nephrectomy and 1 renal endarterectomy. All have had significant reduction of their blood-pressure. At the same time 7 patients with negative tests, but with an obviously small or diseased kidney, have undergone nephrectomy with no reduction in their blood-pressure. Scott reports that they now consider the test positive when there is a reduction of 40 per cent or more in the volume, and 20 per cent or more in the sodium concentration of the urine from one kidney as compared with the other. (In terms of figures quoted in *Table II* this means that in a positive test the volume and sodium concentration on the abnormal side should be less than 60 per cent and 80 per cent respectively of the corresponding values on the normal side.)

Poutasse and others (1958) carried out differential renal function tests in a group of 33 patients, all of whom had had aortography. Of these 33, 11 were considered to have essential hypertension; 6 chronic pyelonephritis, predominantly unilateral; 6 unilateral renal arterial disease; 6 bilateral renal arterial disease; and 4 disease of a segmental branch of a renal artery. They measured urine flow, sodium concentration, and glomerular filtration rate (G.F.R.) by mannitol clearance. They concluded that urine flow was proportional to G.F.R. regardless of the lesion and could therefore alone signify differences in renal function.

Table IV.—Differential Renal Function Studies correlated with Diagnosis

A.—Essential Hypertension

Patient	4	5	10	11	12	19	23	25			Average, per cent
Volume, per cent	91	73	93*	66	89	98	98	86			87*
Sodium concentration, per cent	89	86	107	94	110	70†	92	82			94
Osmolality, per cent		111	92	111	107	111	87	98			102

B.—Chronic Pyelonephritis

Patient	6	8	9	13	18	22					Average, per cent
Volume, per cent	65*	36*	45*	15*	42*	96					50*
Sodium concentration, per cent	82	119	93	275†	84	96					95
Osmolality per cent	42	95	53	93	90	100					79

C.—Renal Vascular Occlusion

Patient	17										Average, per cent
Volume, per cent	9*										9*
Sodium concentration, per cent	66										66
Osmolality, per cent	128										128

Differential function values are expressed as in *Table II*, and represent the side of lower volume shown as a percentage of the side of higher volume.

* These figures may be lower, but not higher.

† Not included in averages owing to liability to inaccuracy.

} *See* footnote to *Table II*.

They also showed that volume and sodium concentration were reduced on the side of unilateral arterial disease, but were also reduced on the more severely affected side in bilateral arterial disease. In segmental arterial lesions, and in pyelonephritis, volumes were reduced on the affected side, but sodium concentrations were variable, being usually lower but sometimes higher than on the normal side. It is perhaps noteworthy that good results, with regard to relief of

FIG. 89.—Aortogram, *Case* 17. The left renal artery is almost completely occluded, while the right one shows definite narrowing at its origin.

hypertension, could be obtained not only in those with unilateral arterial lesions, in which Howard and others' criteria might be fulfilled, but also in segmental arterial lesions, which did not fulfil these criteria.

Schlegel and others (1959) have also reported on their experiences with differential function studies. In 5 patients with hypertension of renal origin who responded to various types of renal or renal vascular surgery, they found a consistent pattern of reduced volume, raised osmolality, and raised potassium and ammonia concentrations. Sodium concentration on the other hand was only reduced more than 10 per cent in 1 case. All these 5 cases had renal vascular abnormalities, and 1 had chronic pyelonephritis also.

The present series includes 6 cases of probable essential hypertension, 8 of probable chronic pyelonephritis, and 1 of occlusive renal vascular disease. Also shown are 1 case with normotension and 1 with, chronic glomerulonephritis. *Table IV* shows the results of differential function studies in these various groups. Obviously it would be premature to draw anything like definite conclusions from these figures, but, nevertheless, it is felt that it is worth recording the findings.

In essential hypertension small variations in the volume produced by the two kidneys were met with, but sodium concentrations and osmolalities remained much the same on the two sides.

In chronic pyelonephritis the volume was usually greatly reduced on the affected side, and osmolality levels tended to be lower than on the normal side, but sodium concentrations were never much reduced and were in fact sometimes increased.

In the case with occlusive renal vascular disease (*Case* 17), a marked lowering of volume and sodium concentration occurred, with a raised osmolality, on the more severely affected side. Incidentally this was the only case in the present series which fulfilled Howard and others' criteria concerning volumes and sodium concentrations, yet it should be noted that aortography demonstrated the presence of bilateral occlusive arterial disease, almost complete on the left, but also present to a lesser extent on the right (*Fig.* 89). In this instance, therefore, Howard and others' test was misleading, since it suggested that left nephrectomy was indicated, and that this could be expected to relieve the hypertension. The knowledge of the bilateral involvement indicated that splenorenal arterial anastomosis was the treatment of choice, but technical difficulties, particularly the arteriosclerotic state of the splenic artery, eventually caused this to be abandoned and nephrectomy was performed. Following operation the hypertension has persisted. According to Poutasse and Dustan (1957) at least 25 per cent of renal arterial occlusive disease is bilateral, so that this would appear to be a serious limitation of Howard and others' test in this type of case.

Certainly the results obtained in this study are in general agreement with those already quoted, but discrepancies exist. Whether these can be ascribed to the differing techniques employed by different surgeons, or whether perhaps, as Schlegel suggests, the pattern of function in a diseased kidney alters as the disease progresses, remain for the present matters of conjecture. It must, however, be remembered that these are comparative tests of renal function, so are only really valid when one kidney is normal. In chronic pyelonephritis it may not be possible to tell whether the disease is wholly or predominantly unilateral, and in occlusive vascular disease aortography is required to determine this point. Furthermore, only aortography can demonstrate segmental arterial lesions.

There seems little doubt, therefore, that differential function studies are capable of yielding certain useful information concerning comparative renal function, so long as their limitations are kept in mind. They cannot, however, be expected to eliminate the need for aortography when renal vascular disease is a possibility, because, although these tests appear to show a consistent pattern in unilateral main artery lesions, they cannot exclude the possibility of its being bilateral; while in segmental vascular lesions their pattern may be difficult to distinguish from chronic pyelonephritis (Poutasse, Donnelly, and Dustan, 1958). In known chronic pyelonephritis, however, a knowledge of the relative volumes and PSP excretion by the two kidneys may be of considerable help in deciding whether or not nephrectomy is advisable.

For the present, therefore, the most useful role of differential function studies would appear to be either as confirmatory evidence of unilateral disease, or to suggest the need for aortography if this is not otherwise indicated, bearing in mind that unilateral disease causing severe hypertension may be present with little or no evidence on pyelography. It still remains to be proven that they are capable of indicating a significant abnormality which cannot be shown by other more reliable means.

SUMMARY

The use of differential renal function studies in the investigation of renal hypertension is discussed, and the experimental basis and technique of these tests are described.

The results of a series of such studies are presented and an attempt made to correlate them with the results of pyelography, aortography, and radioactive diodrast renography.

Reference is made to other published work on this subject, and some proposals are made as to the value and limitations of these tests.

The importance of aortography in selecting those cases of 'essential' hypertension, which are in fact due to renal vascular lesions, is stressed, and criteria for its use suggested.

Acknowledgements.—I would like to express my appreciation and thanks to Dr. Reed M. Nesbit and my colleagues, both medical and surgical, at the University of Michigan Hospital, for all their help and encouragement in this study.

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ARTERIOVENOUS FISTULA FOLLOWING OPERATION FOR PROLAPSED INTERVERTEBRAL DISK

BY R. E. HORTON, BRISTOL

SINCE the first record of an operation for prolapsed intervertebral disk by Mixter and Barr (1934) many thousands of operations have been successfully performed without incident. However, Linton and White (1945) recorded a case in which a fistula between the right common iliac artery and the inferior vena cava had resulted from too deep penetration of an instrument used to remove the disk. Since that time a number of articles have appeared in the American literature which indicate that injury to the great vessels is an occasional complication of the operative treatment of a prolapsed intervertebral disk. The injury may be isolated when an immediate fatality from hæmorrhage is to be expected, but if an artery and vein are simultaneously injured arterial bleeding takes place into the vein so that, although the signs resulting from a major arteriovenous fistula develop, fatal hæmorrhage is less likely.

INCIDENCE OF INJURY TO THE GREAT VESSELS

It is clear that more cases of great vessel injury have occurred than reference to the reported cases would indicate. In his original description Linton mentions 3 which came to his notice as a result of a questionnaire. Holscher (1948) quoted a single case but also knew of 4 unpublished cases of vascular injury after disk operations, and Harbison (1954), after a questionnaire to 100 surgeons, was able to collect notes on 25 cases which had not been reported in addition to 1 case of his own and 4 others which had been reported up to that time. Seventeen of these patients had died, mostly within a few hours of the operation. In 6 cases an arteriovenous fistula had resulted. Only 1 of these patients died, but 2 others had signs of arterial deficiency after ligature operations. Among 24 cases of isolated injury to a great vessel there were 16 deaths (66 per cent). Since this summary Seeley, Hughes, and Jahnke (1954) have recorded 2 more cases of injury to the common iliac artery (one right and the other left). Early operation saved both of these patients, though one had a complicated recovery. Nine further cases of arteriovenous fistula have been described following operation for prolapsed intervertebral disk. One of these was diagnosed at autopsy (Fortune, 1956), but the others recovered after corrective operations (Smith, Hughes, Sapp, Joy, and Mattingly, 1957 (2); De Bakey, Cooley, Morris, and Collins, 1958 (2); Glass and Ilgenfritz, 1954 (1); Kirklin, quoted by Burchell, 1954 (1); Mack, 1956 (1); and Harbison, 1954 (1)).

AETIOLOGY

The emphasis on the importance of complete removal of the disk by Dandy, and now generally practised, must have made vascular injury more likely. It is also possible that the prone position makes the vessels more vulnerable. It has been observed, too, that the injury can occur at the hands of an experienced and gentle surgeon, and the words of Holscher (1948) have often been quoted. He describes how an experienced surgeon was 'sounding' for the anterior portion of the annulus fibrosus with a *closed* pituitary rongeur when, "... with surprising ease, it slipped through the interspace. As the instrument was

withdrawn a copious welling up of dark blood immediately occurred in the joint." Holscher continues, ". . . the ease with which this complication can occur can only be appreciated by the surgeon in whose hands such an unfortunate accident has happened".

This case and the experience of others suggests that the injury takes place when there is a defect in the annulus which permits the passage of an instrument into contact with the great vessels, without the use of such force as would be expected to be necessary to penetrate the normal annulus. The great vessels are relatively fixed and are easily penetrated rather than pushed aside by an instrument. Leavens and Bradford (1953) described such a defect and, after passing an instrument through it, injected radio-opaque fluid and showed that it lay in front of the vertebral bodies.

Knowledge that this defect can be present and the ease with which the great vessels can be damaged is probably their most important safeguard.

Case 1.—Mrs. P., a woman of 46 years, had had backache and sciatica for some three years. A diagnosis of prolapsed intervertebral disk was made and on Feb. 10, 1959 she was operated on by an experienced senior registrar. Fenestration of the disk between the 5th lumbar and 1st sacral vertebræ showed it to be normal. The disk between the 4th and 5th lumbar vertebræ was found to be prolapsed and was thoroughly evacuated. There was no unusual blood-loss at the time of the operation but at its completion her condition was not good. The blood-pressure was 90/50 and the anæsthetist considered that she was in a state of surgical shock not due to blood-loss. Accordingly a noradrenaline infusion was started but she continued in poor condition, with tachycardia and pallor. About six hours after the operation it was noted that the abdomen was tender and rigid and bowel-sounds were absent. The femoral pulses were collapsing. Two days later a loud systolic murmur was heard in the lower abdomen and a thrill was palpable over the right femoral artery. An aortogram performed six days after the operation showed that a fistula was present, but the flow was too great for its accurate localization.

She was re-explored seven days after the first operation. A long paramedian incision was made and the great

Table I.—Summary of Cases

No.	Author	Operation Date	Operation Signs	Early Post-operative Signs	Late Signs	Anatomy	Treatment	Time	Result
1	Linton and White	1945	None	None	Cardiac failure 4 mth.	R.C.I.A./I.V.C.	Ligation	4 mth.	Good
2	Holscher	1948	Bleeding + + No shock	Throbbing pain and ileus. Post-operative thrill	—	R.C.I.A. and V.	Quad. ligation	6 mth.	Good. Some swelling of leg
3	Fortune	1953	—	Abdominal distension	Circulatory failure at 3 mth.	L.C.I.A. and V.	Died during investigation of cardiac failure	—	Diagnosed at post-mortem
4	Glass and Ilgenfritz	1954	No bleeding. Shock when patient put on back at end of operation	Thrill immediately. Ileus	1 mth. signs of left ventricle failure	I.V.C. R.C.I.A.	Quad. ligation I.V.C. and R.C.I.A.	10 wk.	Satisfactory
5	Harbison	1954	Moderate bleeding	None	Cardiac failure at 5 mth. Thrill	L.C.I.A. and V. Huge aneurysm too	Repair	5 mth.	Good
6	Kirklin (quoted by Burchell)	1954	—	—	—	Aorta/I.V.C.	Aortic graft	—	Good
7	Mack	1956	None	None	Cardiac failure 3 wk.	R.C.I.A./I.V.C.	Ligation R.C.I.A.	7 wk.	
8	Smith and others	1957	Increased bleeding	Dyspnœa on ambulation (9th day). Congestive failure by 14th day	—	R.C.I.A. and V.	Repair	28 d.	Good
9	,,	1957	No extensive blood-loss but loss of pulse and B.P. Restored with blood transfusion (rapid)	Tightness in chest. Abdominal pain. Orthopnœa. B.P. 130/40. Signs of cardiac failure by 7th day	—	L.C.I.A. and V.	Repair	39 d.	Good
10	De Bakey and others	1958	—	—	Tiredness 2 yr. after disk operation. Machinery murmur and thrill in abdomen	Aorta/I.V.C. just above bifurcation	Repair	2 yr.	Good
11	,,	1958	—	—	Dyspnœa and palpitation 6 mth. after operation. Murmur and thrill +	,,	Repair and graft to L.C.I.A.	8 mth.	Good

vessels exposed. Proximal control of the aorta was obtained with a tape and later with a Potts multi-tooth clamp. Distal control of both common iliac arteries was effected with bulldog clamps. In dissecting in the region of the fistula a small aneurysm sac was opened and considerable venous bleeding took place as the veins had not yet been vein was ligated. Fixation by fibrosis made it dangerous to encircle the vena cava completely but as much as possible was contained in a Potts clamp. Control of the circulation having been obtained, dissection was begun between the left common iliac vessels proximal to the fistula and a second bulldog clamp was placed on the

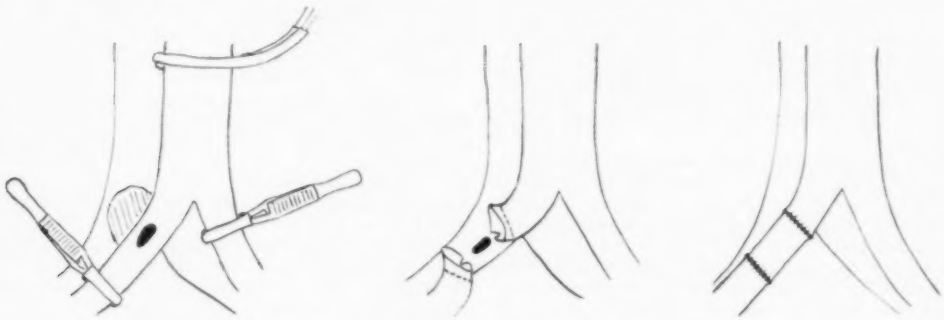

FIG. 90.—*Case* 1. A, Shows the position of the fistula and the preliminary controls. B, Division of the common iliac artery to display the opening into the vein. C, Insertion of homograft after trimming of the ends of the common iliac artery.

controlled. It was necessary to transect the right common iliac artery to gain access and then the common iliac vein was repaired without securing control. The ends of the common iliac artery could not be brought together and a homologous artery graft about 2 cm. long and of somewhat smaller calibre was inserted (*Fig.* 90). A 6-pint blood transfusion was given during this operation. The anæsthetist noted an immediate fall in the pulse-rate when the circulation was restored. The right leg swelled after the operation and it was thought that this was due to thrombosis of the damaged common iliac vein. Four weeks after the operation she suffered a pulmonary embolus, but was fit for discharge ten days later. Fifteen months later she was in excellent health and the only abnormality to be noted was a systolic murmur heard in the right iliac fossa. This is due to the fact that the graft is somewhat narrower than the iliac artery into which it was sutured.

Case 2.—A man of 56 years had an operation for a prolapsed intervertebral disk in 1952. There was an unusual amount of bleeding and he required a blood transfusion. However, nothing untoward was noted until a cholecystectomy was performed in 1958. It was then observed that there was a very loud thrill over the inferior vena cava. He was also complaining of dyspnœa and a feeling of "pumping all over". There was a loud murmur and palpable thrill all over the abdomen, but maximal over the left iliac fossa. The blood-pressure was 160/60. A chest radiograph showed enlargement of the heart and some pulmonary congestion due to left heart failure. An aortogram showed the aorta and iliac arteries with simultaneous filling of the great veins, which were greatly dilated. The exact position of the fistula was not shown.

The great vessels were explored through a long paramedian incision in July, 1959, seven years after the operation which had resulted in the fistula. Proximal control of the aorta was achieved with a Potts multi-tooth clamp. On the right side the common iliac artery and vein were isolated and occluded with a single Potts clamp. There was a good deal of fibrosis and fixation of the vessels as a result of the extravasation of blood which had taken place at the time of the injury. The left common iliac artery was isolated and controlled with a bulldog clamp just distal to the fistula. The left common iliac vein was very greatly distended. The left external iliac vein was controlled with an encircling ligature and the internal iliac common iliac artery just below the aortic bifurcation. It was now possible to identify the fistula and to divide it. The common iliac vein was repaired and all the clamps except those on the left common iliac artery adjacent to the fistula were removed. The hole in the artery was irregular, but it was closed with interrupted sutures and

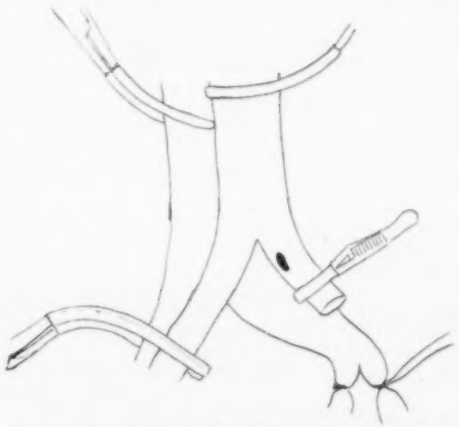

FIG. 91.—*Case* 2. This indicates the position of the fistula and the controls which were used.

the remaining clamps were removed (*Fig.* 91). The patient left hospital 17 days after operation and was well when seen later. He had no dyspnœa and the sensation of continuous pumping had gone. The blood-pressure was 135/70. There were no local signs.

SIGNS OF VASCULAR DAMAGE

When there is isolated injury to the aorta or to one of the iliac arteries serious bleeding is inevitable. Its outward manifestation may be slight, but severe retroperitoneal bleeding will be accompanied by surgical shock, and if blood transfusion does not

rapidly restore the blood-pressure there seems little doubt that immediate exploration of the great vessels is the only measure which gives the patient any hope of survival.

Thirteen cases (including 2 described in this paper) of arteriovenous fistula following an operation for prolapsed intervertebral disk have now been described in the literature. In 3 cases the records do not give any account of the symptoms and signs which followed the disk operation. In 3 cases there seems to have been no indication of bleeding at the time of the operation, but in the other 7 there was either moderate external bleeding, severe surgical shock, or both.

Early post-operative signs that an arteriovenous fistula has resulted include ileus and interference with micturition. Deep abdominal tenderness and the development of a murmur and thrill were noted early in nearly all cases.

The time of onset of cardiac failure was variable and presumably depended on the size of the shunt and the amount of cardiac reserve. It may come on as early as a week after the operation or be delayed for some years. In a number of cases the onset of cardiac failure was the first sign that an arteriovenous fistula had resulted from the disk operation.

TREATMENT

Operations directed to treatment of the fistula have been done at varying times, but the 2 cases described here are the earliest (7 days) and latest (7 years) after a disk operation that have been recorded.

The onset of cardiac failure is a clear indication that closure of the fistula is an urgent necessity.

One patient died during investigation and 4 were treated by ligature operations to exclude the fistula. There is no doubt that ligature of the common iliac artery above and below a fistula will result in little impairment of circulation to the corresponding foot as the collateral circulation is excellent, and in all the cases in which this was done a good result was recorded. Ligature or thrombosis of the iliac vein, however, is likely to be followed by œdema of the leg, which may be troublesome.

In the 8 further cases reconstructive operations were performed, though in 3 of these it was necessary to introduce an arterial graft. Excellent results followed in all the recorded cases in which this was done.

SUMMARY

It is possible to damage the great vessels during an operation for prolapsed intervertebral disk, and the ease with which the accident may happen is emphasized.

The previously reported cases have been reviewed and 2 additional cases are described.

I wish to express my thanks to Dr. D. H. Davies who diagnosed *Case* 2 and referred the patient to me.

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PRIMARY MALIGNANT LYMPHOID TUMOURS OF THE INTESTINAL TRACT

REPORT OF 37 CASES WITH A STUDY OF FACTORS INFLUENCING PROGNOSIS

BY I. M. P. DAWSON, J. S. CORNES, AND B. C. MORSON

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MALIGNANT tumours of lymphoid tissue affecting the alimentary tract have been recognized for more than a hundred years, and well over 600 cases involving the small and large intestine are now on record. Unfortunately, many of these cases are poorly documented, and are of little help to anyone making a critical study of these tumours.

Firstly, at least a third of the recorded cases are not certainly primary neoplasms of the intestinal tract, although they are often listed as such in the titles of the papers because the earliest and most important symptoms were referable to the bowel or because the intestinal lesions appeared larger and more important than the other lesions found at laparotomy or necropsy. The possibility that such intestinal lesions might in fact have been part of a more generalized disorder was not often mentioned, and very few papers stated the criteria used in making the diagnosis of a malignant lymphoma primarily situated in the intestinal tract.

Secondly, the term 'lymphosarcoma' has been used by many writers to indicate any or all of the

varieties of malignant tumours of lymphoid tissue, and the finer distinctions of giant follicular lymphoma, Hodgkin's disease, and reticulum-cell sarcoma have been ignored.

Thirdly, before 1950, benign lymphoid polyps of the rectum were not generally recognized as such and were often called 'lymphosarcomas'. Some of these cases have been included in published series of malignant lymphomas of the gastro-intestinal tract, which explains some of the long-term survivals recorded in the literature (Helwig and Hansen, 1951).

Fourthly, many of the large series of cases reported in the literature give little individual case data, simply summarizing the main findings in general tables. Because these tables are usually unrelated, it is virtually impossible to trace a particular case from one table to another. The subject is further confused by some cases being published several times in different journals, or by being republished in ever-enlarging series from the same medical centre.

Lymphoid tumours have been reported more frequently in the stomach than in the intestinal tract. Friedman (1959), for example, has reported a series of 75 gastric cases from the Mount Sinai Hospital, New York, and similar large series have been published by Madding and Walters (1940), 47 cases; Allen, Donaldson, Sniffen, and Goodale (1954), 44 cases; Thorbjarnarson, Pearse, and Beal (1959), 37 cases; Snoddy (1952), 34 cases; Warren and Littlefield (1955), 30 cases; Wolferth, Brady, Enterline, and Blakemore (1959), 26 cases; and by others. Very few large series of malignant intestinal lymphoid tumours have been published. Faulkner and Dockerty (1952) described 33 cases seen at the Mayo Clinic, and similar series have been published by Allen and others (1954), 34 cases; Raiford (1933), 32 cases; Warren (1959), 24 cases; Marcuse and Stout (1950), 13 cases; and by others. There are very few cases recorded in the British literature. Skrimshire (1955) described 14 cases from St. Thomas's Hospital, London; Irvine and Johnstone (1955) 17 cases seen at the Western Infirmary, Glasgow; Ogilvie and Shaw (1955) 5 cases seen at the Essex County Hospital, Colchester; and Azzopardi and Menzies (1960) 10 cases from the Postgraduate Medical School, London.

No one centre can hope to see enough primary intestinal cases to be able to lay down any generally useful prognostic criteria, or to arrive at any definite conclusions about the best methods of treatment. Only through the publication of essential individual case data is it possible for one centre to share its results with others. For these reasons we wish to set on record the essential data from a series of 37 cases of primary malignant lymphoid tumours of the intestinal tract from three major centres, to review well-documented primary cases recorded in the literature, and to consider some of the factors which appear to influence prognosis.

MATERIALS AND METHODS

The 37 cases to be described were found during a search through the pathology reports of St. Mark's and Westminster Hospitals for the past twenty-five years, and the Gordon Hospital since its re-opening in 1947. The tumours were considered clinically to be primary in the intestine on the following grounds:—

1. When the patients were first seen there was no palpable superficial lymphadenopathy.
2. Chest radiographs showed no obvious enlargement of the mediastinal lymph-nodes.
3. The white-blood cell-counts, total and differential, were within normal limits.
4. At laparotomy the bowel lesion predominated, the only lymph-nodes obviously affected being those in its immediate neighbourhood.
5. The liver and spleen appeared free of tumour in every case.

Some cases were found in which the retroperitoneal lymph-nodes were affected as well as the mesenteric lymph-nodes and bowel. We excluded all these cases from our study since the primary lesion might well have been in the abdominal lymph-nodes rather than in the bowel.

Adequate follow-up data were obtained in 34 of the 37 cases. In 33 cases operation specimens were available for study, and in 7 necropsy specimens were also available. In the 4 remaining cases the diagnoses were based on the results of sigmoidoscopies, barium enemas, rectal biopsies, lymph-node biopsies, and the findings at laparotomy. Material for histological study was fixed in 10 per cent formol saline and embedded in paraffin. Sections were stained using Erhlich's hæmatoxylin and 0·25 per cent alcoholic eosin, and Gordon and Sweets's (1936) silver impregnation technique was used to demonstrate reticulin. The cases were then classified into giant follicular lymphoma, lymphosarcoma, Hodgkin's disease and Hodgkin's sarcoma, reticulum-cell sarcoma, as described by Harrison (1953).

In excluding benign rectal lymphomas from this series we required that such tumours should be entirely within the mucosa and submucosa, that there should be no invasion of the underlying muscle coats, and that there should be at least two discrete germinal follicles present. If the rectal biopsies failed to include the muscle coats, and no germinal follicle was seen, the biopsies were regarded as inconclusive. The diagnosis of a primary malignant rectal lymphoma was only made when the muscle coats were clearly invaded by a tumour mass, and in none of these cases was any follicular pattern seen. The principal findings in 87 cases of benign rectal lymphoma seen at St. Mark's Hospital have been summarized by Morson (1959).

A detailed study of cases reported in the literature has been made, and 142 intestinal cases have been found where there was sufficient individual case data to indicate that one was dealing with a primary bowel lesion. Only those cases stating the age and sex of the patient, the site and cell type of the tumour, the type of treatment given, and sufficient clinical data for the diagnosis of a primary lesion and for provisional follow-up were chosen. For comparison, 117 primary malignant lymphomas of the stomach, similarly recorded in the literature, have also been studied.

Our 37 intestinal cases, together with the 142 intestinal cases and the 117 gastric cases collected from the literature, form the basis of this report.

RESULTS

Thirty-seven Intestinal Cases studied in Our Own Laboratories.—

General Data.—The most important data from 37 cases of primary malignant lymphomas of the intestinal tract are given in *Table I*. The age given is the age at onset of the disease when this could be determined, and if not, the age at diagnosis. The length of survival recorded is the duration from the date of resection or commencing radiotherapy, or from the time of diagnosis when no specific treatment was given.

Symptoms and Signs.—The chief presenting symptoms and signs are summarized in *Table II*. The small intestinal tumours most commonly presented with nausea, vomiting, and other signs suggesting intestinal obstruction, and a mass was often palpable in the abdomen. Growths in the colon and rectum most often presented with bleeding and altered bowel habits, and growth was often visible on proctoscopy or sigmoidoscopy. In 3 of the 4 patients with multiple lymphomatous polyposis, the polyps were both seen and felt in the rectum. In 13 out of our 37 cases there was no complaint other than a feeling of malaise until the sudden onset of obstruction (11 cases) or perforation (2 cases) necessitated surgical intervention.

FIG. 92.—Ileum, cæcum, and ascending colon. Bulky protuberant growth (reticulum-cell sarcoma) of cæcum. (*Case* 17.)

FIG. 94.—Ileum, cæcum, and ascending colon. Aneurysmal ileal growth (reticulum-cell sarcoma). (*Case* 9.)

Macroscopical Appearances.—In 33 of the 37 cases the tumours were discrete. In 27 of these the tumours were single, and in 6 cases two or more tumours were present. Macroscopically, the discrete tumours appeared to be of three types: 11 were bulky protuberant growths (*Fig.* 92); 21 were annular or plaque-like thickenings of the bowel wall (*Fig.* 93); and 1 presented as an aneurysmal dilatation of the terminal ileum (*Fig.* 94). In the 4 remaining cases

FIG. 93.—Descending colon, sigmoid colon, and rectum. Two separate annular growths (lymphosarcomas) in recto-sigmoid region. Note smooth appearance of colon due to quiescent ulcerative colitis. (*Case* 21.)

FIG. 95.—Transverse, descending, and sigmoid colon. Multiple lymphomatous polyposis (giant follicular lymphoma pattern). (*Case* 34.)

the tumours presented as a multiple lymphomatous polyposis affecting long segments of the intestinal tract (*Fig.* 95). Further details of these 4 cases have been published elsewhere (Cornes, 1961). There was no tendency for any one histological type of tumour to be associated with any particular macroscopical appearance, to produce multiple tumours or lymphosarcomas penetrating the muscle coats, with the sigmoid growth extending outwards into the pericolic fat (*Fig.* 93). A more detailed description of this case is available elsewhere (Cornes, Smith, and Southwood, 1961).

One case (No. 26) had a large lymphocytic lymphosarcoma of the rectum with a small

Table I.—Data from 37 Cases of Primary Malignant Intestinal Lymphoid Tumours

Case No.	Sex	Age	Location	Number of Tumours	Cell Type	Regional Lymph-nodes Involved	Surgical Removal	Radio-therapy	Outcome				
									Local Recurrence	Systemic Disease	Patient Dead	Survival yr.	Survival mth.
1	M.	89	J	S	LS	0	+	0	+	0	A	1	10
2	M.	62	J and I	M	LS	?	+	0	0	0	D		0
3	M.	48	J and I	M	LS	+	+	+	+	0	D	16	4
4	M.	47	J and I	M	LS	+	+	+	+	0	A	6	1
5	M.	41	I	S	RS	?	+	0	+	0	D	3	0
6	M.	49	I	S	LS	0	+	+	0	+	D	3	6
7	M.	52	I	S	LS	?	+	+	0	+	D	2	0
8	F.	50	I	S	RS	+	+	+	0	0	D		1
9	M.	58	I	S	RS	?	+	+	+	+	D		2
10	M.	41	I	S	RS	+	+	+	0	0	A		11
11	F.	56	I	S	HD	?	+	+	0	+	D		4
12	F.	24	I	S	RS	?	+	0	?	?	?		?
13	M.	54	IC	S	RS	+	+	0	0	0	D		8
14	M.	59	IC	S	LS	+	+	+	+	0	A	4	2
15	M.	18	IC	S	RS	?	+	+	0	0	A	1	5
16	M.	60	C	S	HD	0	+	0	?	?	?		?
17	M.	52	C	S	RS	0	+	+	0	0	A	2	1
18	F.	71	C	S	RS	0	+	0	0	+	D	1	4
19	M.	29	C	S	HD	?	+	0	?	?	?		?
20	M.	60	C and R	M	LS	0	+	0	0	0	A	15	0
21	F.	42	C and R	M	LS	0	+	0	+	0	A	1	2
22	M.	44	R	S	RS	?	0	0	0	+	D		10
23	F.	57	R	S	LS	0	+	0	0	0	A	15	3
24	F.	65	R	S	RS	+	+	+	0	+	D		7
25	F.	61	R	S	RS	+	+	0	0	0	D		0
26	M.	57	R	S	LS	0	+	+	0	0	D	1	0
27	M.	65	R	S	LS	+	+	0	0	0	A		4
28	M.	54	R	S	LS	?	0	+	0	+	A	3	2
29	F.	36	R	S	LS	?	+	+	+	0	A	17	6
30	F.	35	R	S	RS	+	+	0	0	+	D		10
31	F.	66	R	S	LS	+	+	0	0	0	A	2	6
32	F.	53	R	S	HD	0	+	+	0	0	A	1	9
33	F.	54	R	M	LS	0	+	+	0	+	D	1	5
34	M.	75	D–R	MP	GF	+	+	0	–	+	A	1	10
35	F.	44	D–R	MP	LS	+	0	+	–	+	D	2	6
36	M.	51	J–I	MP	HD	0	+	0	–	0	D		2
37	M.	50	C–R	MP	LS	?	0	+	–	+	A	3	3

C, Colon; D, Duodenum; I, Ileum; IC, Ileocæcal; J, Jejunum; R, Rectum; S, Single tumour; M, Multiple tumours; MP, Lymphomatous polyposis; GF, Giant follicular lymphoma; HD, Hodgkin's disease; LS, Lymphosarcoma; RS, Reticulum-cell sarcoma.

diffuse polyposis, or to show a predilection for any one site.

Lymph-nodes.—The finding of enlarged mesenteric lymph-nodes at operation did not necessarily indicate involvement by tumour or that the intestinal growths were inoperable. In 4 cases surgeons reported enlarged lymph-nodes at operation, but no tumour was found when the lymph-nodes were sectioned and examined histologically. In 5 cases no enlarged lymph-nodes were seen at operation, and none were found when the specimens were examined in the laboratory, yet tumour was found histologically in each case. In only 8 cases was the finding of enlarged lymph-nodes at operation actually associated with their involvement by growth.

Associated Disorders.—One case (No. 21) complicated a chronic ulcerative colitis. This patient gave a fifteen years' history of intermittent diarrhœa and bleeding. At laparotomy two tumours were found, one in the sigmoid colon and one in the rectum. Sections showed a chronic, quiescent ulcerative colitis affecting the whole colon, and two lymphocytic

Table II.—Major Presenting Symptoms and Signs in 37 Cases of Primary Malignant Intestinal Lymphomas

	Small Intestinal Cases	Large Intestinal Cases	Multiple Lymphomatous Polyposis	Total
Bleeding per rectum	1	8	2	11
Severe abdominal pain, nausea, and vomiting	8	1	0	9
Malaise, vague pains, etc.	5	7	2	14
Symptoms not stated	1	2	0	3
Visible growth in rectum	0	12	3	15
Palpable abdominal mass	5	2	1	8
Signs of obstruction	8	2	1	11
Signs of perforation	2	0	0	2
Signs not stated	2	2	0	4

mucus-secreting adenocarcinoma immediately below it at the anorectal junction. In a second case (No. 7) resection of a lymphocytic lymphosarcoma of the terminal ileum was followed one year later by the development of an adenocarcinoma of the sigmoid colon. In a third case (No. 17) resection of a reticulum-cell sarcoma of the ascending colon was followed eighteen months later by the development of five separate carcinomas of the rectum and sigmoid colon. Further details of these three cases have been given elsewhere (Cornes, 1960). A fourth case (No. 3) died sixteen years after the resection of multiple lymphocytic lymphosarcomas of the jejunum and ileum. At necropsy there was a carcinoma of the upper lobe of the left lung, but no evidence of any lymphosarcoma.

Study of Primary Cases recorded in the Literature.—

Survival Studies.—We have attempted to extend our observations by a study of similar cases recorded in the literature. *Table III* gives the follow-up data on 176 intestinal cases and 117 gastric cases. The 176 intestinal cases include 34 cases from our present study and 142 cases collected from the literature. The table shows that about half of the recorded intestinal cases have been followed for less than 1 year, and that very few cases have been followed for 10 years. Most of the recorded deaths were in the first year. None of the deaths occurring after 10 years were due to the original disease, and there is no record of any of these patients surviving more than 10 years with evidence of recurrent disease. Several patients who survived 5 years had clinical evidence of either a local recurrence or a systemic spread of their disease, and some of the recorded deaths in the 5–10-year period were due to the original disease.

Table III.—Follow-up Data on Recorded Cases of Primary Malignant Lymphomas

Site and Cell Type	Total Number of Cases	Survival (in years)								
		0–1			1–5		5–10		10 *plus*	
		Total	Dead	Death due to Operation	Total	Dead	Total	Dead	Total	Dead
Intestinal:—										
Giant follicular lymphoma	12	1	1	0	5	0	6	1	—	—
Lymphosarcoma	85	41	31	6	23	10	11	1	10	1
Hodgkin's disease	15	9	7	1	6	0	—	—	—	—
Hodgkin's sarcoma	4	4	3	0	—	—	—	—	—	—
Reticulosarcoma	60	30	24	8	23	8	4	1	3	0
	176	85	66	15	57	18	21	3	13	1
Gastric:—										
Lymphosarcoma	45	8	7	0	9	1	14	3	14	2
Hodgkin's disease	19	7	5	2	6	2	5	0	1	0
Hodgkin's sarcoma	3	0	0	0	1	0	2	1	—	—
Reticulosarcoma	50	15	10	2	15	7	14	1	6	2
	117	30	22	4	31	10	35	5	21	4

Seven intestinal and 5 gastric cases died from causes unrelated to their original disease.

Follow-up Studies.—Of 34 cases with follow-up data available, 17 are dead. Three deaths were due to post-operative complications, 3 were due to other causes, and 11 deaths were directly due to the disease. Of 17 survivors, 7 have either a local recurrence or are suffering from generalized disease, and 10 patients are alive, well, and apparently free from recurrent disease. Taking all the available results into consideration it would appear that not more than one-quarter of all cases will survive ten years from the time of diagnosis.

Table IV.—Uncorrected 5-year and 10-year Survival Figures of Recorded Cases of Primary Malignant Lymphoma

Site and Cell Type	Percentage 5-year Survival	Percentage 10-year Survival
Intestine:—		
Giant follicular lymphoma	50	?
Lymphosarcoma	25	12
Hodgkin's disease	None	None
Reticulosarcoma	11	5
Gastric:—		
Lymphosarcoma	62	31
Hodgkin's disease	31	?
Reticulosarcoma	40	12

Table V.—Influence of Age on Length of Survival in Cases of Primary Malignant Intestinal Lymphomas

Survival (years)	Age at Onset			
	Under 20		*Over* 40	
	Total	Dead	Total	Dead
0–1	15	12	54	42
1–5	9	2	39	12
5–10	6	0	15	2
10 plus	2	0	8	0
	32	14	116	56

Table IV gives the uncorrected 5-year and 10-year survival figures for the cases listed in *Table III*. These percentages are based simply on the total number of cases studied, the number of patients surviving the 5-year and 10-year periods, and the total number of deaths. They do not include the patients who are alive, but who have not been

followed for the 5-year and 10-year periods. These figures therefore give a gloomier picture of these disorders than corrected survival figures would give.

Age and Sex.—Age at onset did not appear to have any significant influence upon the site of intestinal lesions. Thirty-two of the 176 intestinal cases under review occurred in patients under the age of 20 years, and 116 cases occurred in patients over the age of 40 years. These cases are compared in *Table V*, where it will be seen that the overall prognosis is slightly better in the under-20 group, and if the cases surviving more than one year are considered the outlook appears even more favourable. The majority of the tumours found in young people were lymphosarcomas; 26 of the 32 cases were of this type, 5 were reticulum-cell sarcomas, and 1 was a giant follicular lymphoma (Marcuse and Stout, 1950). There was no case of primary Hodgkin's disease or Hodgkin's sarcoma in the under-20 age-group, and none of the primary reticulum-cell sarcomas occurred in children under the age of 10 years.

Table VI.—Data from 8 Recorded Cases of Primary Malignant Duodenal Lymphomas

Authors	Resection	Radiotherapy	Survival (mth.)
Kaplan, Tyler, and Canale	+	0	0
Case, Ribando, and Halstead	+	0	7
Jackson and Parker	0	0	3
Skrimshire	0	0	3
Marcuse and Stout	0	0	5
Skrimshire	0	+	10
Marcuse and Stout	0	+	13
Marcuse and Stout	0	+	44

Primary malignant intestinal lymphomas are approximately twice as common in men as in women. One hundred and fifteen cases occurred in males, and 61 in females. Under the age of 20 years, males outnumbered females by more than three to one, 25 cases occurring in males, and 7 in females. No other significant relationship could be found between sex, site of tumour, cell type, or length of survival.

Site and Cell Type of Lesion.—Tables III, IV suggest that lesions in the stomach have a better prognosis than intestinal lesions. Lesions in the duodenum have a poor prognosis compared with similar lesions in other parts of the intestinal tract. Eight well-documented primary duodenal cases recorded in the literature are summarized in *Table VI*. In the second case in the table the patient was reported to have survived the immediate post-operative period, but no further follow-up details were given. The remaining cases were all dead. Apart from the duodenum, the situation of lesions in other parts of the intestinal tract did not appear to have any significant influence upon prognosis, and there was no good evidence to suggest that cæcal lesions necessarily had any better prognosis than similar lesions elsewhere (*see Table VII*) (Usher and Dixon, 1943). Giant follicular lymphomas and lymphosarcomas appear to have a better prognosis than Hodgkin's disease, Hodgkin's sarcoma, or reticulum-cell sarcoma.

Multiple Tumours.—The gastro-intestinal tract is often secondarily involved in generalized malignant lymphomatosis, and in such cases the tumour deposits are usually multiple, and may be fairly widespread. These cases are usually associated with a bad prognosis. Multiple primary growths other than lymphomatous polyposis also occur and were found in 18 of the intestinal cases under review. Five of these cases survived 5 years, and 3 survived for 10 years or more. When strict criteria are used for the diagnosis of primary malignant intestinal lymphomas, there is no good evidence that these multiple tumours have a worse prognosis than the solitary neoplasms.

Table VII.—Data from 9 Recorded Cases of Primary Malignant Cæcal Lymphomas

Authors	Surgical Removal	Radiotherapy	Local Recurrence	Alive or Dead	Survival	
					yr.	mth.
Jackson and Parker	+	0	—	D		0
Erbes and Stehlin	+	+	0	A		4
D'Alonzo	+	0	0	A		5
Warren and Lulenski	+	?	+	D		6
Portmann, Dunne, and Hazard	+	+	+	A		8
Pattison	+	0	+	A	2	3
Warren and Lulenski	+	0	0	A	5	0
Bresnihan	+	0	0	A	6	9
Azzopardi and Menzies	+	+	0	A	15	3

Lymph-nodes.—The influence of regional lymph-node involvement on prognosis was difficult to assess. Thirty-four of the gastric and intestinal cases under review survived for 10 years. In 8 cases the histology of the regional lymph-nodes was not recorded, in 18 cases the nodes were said to be free from involvement, and in 8 cases the nodes were said to be involved. Regional lymph-node involvement does not therefore preclude the chance of a long survival.

Treatment.—Of 13 intestinal cases surviving 10 years, 4 were treated by surgery alone, and 9 by surgery and radiotherapy. We could find no well-documented record of any primary intestinal case treated solely by radiotherapy surviving for 10 years. Too few cases have been recorded to assess the influence of radiotherapy, but from the data available it was not obvious that radiotherapy significantly lengthened a patient's chance of survival. It did, however, produce a remarkable clinical improvement in a number of cases, and there were several reports of the striking reduction in size of abdominal masses, alleviation of obstructive symptoms, and improvement in the patient's sense of well-being.

DISCUSSION

Selection of Cases.—Since malignant tumours of lymphoid tissue often originate in the retro-peritoneal lymph-nodes it is not surprising that gastro-intestinal tract involvement is seen in at least 10–20 per cent of all cases of malignant lymphoid tumour (Gall and Mallory, 1942). Willis (1953)

found that nearly two-thirds of his cases of lymphosarcoma appeared to originate in the abdominal lymph-nodes. These findings probably account for the many hundreds of cases of malignant lymphoid tumour affecting the gastro-intestinal tract recorded in the literature. Unfortunately, very few papers have stated the criteria used in making this diagnosis and it is therefore difficult to recognize which cases are primary lesions and which are not. Because several well-known reviews of the literature include a number of cases which are not apparently primary bowel tumours, their discussions of the factors which appear to influence the prognosis of primary bowel lesions are of questionable value.

Only primary lesions of the stomach and intestines have been referred to in this study, and where there was any doubt about a recorded case it has not been included. We have not used the large series recorded by Balfour and McCann (1930), Madding and Walters (1940), Usher and Dixon (1943), McSwain and Beal (1944), Spellberg and Zivin (1949), Marshall and Meissner (1950), Faulkner and Dockerty (1952), Crile, Hazard, and Allen (1952), Burman and van Wyk (1955), Hunt, Broders, and Hightower (1958), Thorbjarnarson and others (1959), Jackson and Coady (1959), or Warren (1959) because these papers give only general information, and do not provide individual case data. We have not used the cases reported by Raiford (1933), or by Patterson, Callow, and Ettinger (1958), because of our uncertainty about the cell types described. We have not used the Lahey Clinic series reported by Warren and Littlefield (1955) because the age and sex of the patients were not given, and because they included a group of 'unclassified lymphomas' which had a surprisingly good prognosis. In our experience 'unclassified lymphomas' have a very bad prognosis because they are usually anaplastic sarcomas which we find difficult to classify as Hodgkin's sarcoma, reticulum-cell sarcoma, or lymphoblastic lymphosarcoma (*see also* Lumb, 1954). Inevitably some cases have been overlooked and the selection of cases for publication may not fully reflect the general behaviour of these tumours since some were published simply to illustrate cases of long survival and others to illustrate features of small-bowel tumours. Despite these and other limitations, however, certain features emerge which appear to have some significance.

Influence of Site.—Primary malignant lymphomas of the gastro-intestinal tract are found most frequently in the stomach. In the intestines these tumours are found most frequently in the ileum. Apart from the cæcum, large-intestinal lesions are uncommon. The large number of cases affecting the rectum and sigmoid colon in our series of 37 cases simply reflects the specialized work of St. Mark's Hospital and the Gordon Hospital in the field of colonic and rectal surgery, and the large number of cases referred to these centres from different parts of the world.

Gastric lesions appear to have a better prognosis than similar lesions in the intestines, probably because they give rise to symptoms earlier, are easier to diagnose, and are more amenable to surgery. Duodenal lesions appear to have a bad prognosis because of their special situation, and the technical difficulties of surgical removal. The situation of lesions in other parts of the intestinal tract does not appear to influence the patient's length of survival after treatment. Usher and Dixon (1943), Marshall and Meissner (1950), Lockwood (1952), and Azzopardi and Menzies (1960) have all suggested that cæcal lesions have a better prognosis than similar lesions in other parts of the intestinal tract, whilst Allen and others (1954) and Warren and Littlefield (1955) have suggested that they have a worse prognosis. These differences of opinion are probably due to the small number of cases studied. Our study includes 9 cæcal tumours, and we could find no significant evidence that these tumours behaved any differently from similar lesions in other parts of the large intestine, jejunum, or ileum.

Multiple Tumours.—It is often suggested that multiple primary tumours have a worse prognosis than single tumours. Many reviews include tumours which are not primary bowel lesions: when strict criteria are used in the diagnosis of a primary bowel lesion there is no good evidence that multiple lesions do have a worse prognosis. Faulkner and Dockerty (1952) found that multiple primary growths had a better prognosis after resection than single growths, and in our own series multiple lesions had a similar prognosis to the single ones.

Multiple lymphomatous polyposis is an unusual condition in which sessile or pedunculated polyps composed of varying types of lymphoid tissue involve considerable segments of the gastro-intestinal tract. In the majority of cases the polyps extend from the pyloric end of the stomach to the anorectal junction. Because of the extensive gastro-intestinal tract involvement radical surgery is impossible, and such cases have therefore got a bad prognosis. In a recent study of 27 cases (Cornes, 1961) the majority of 7 patients were dead within 2–3 years from the time of diagnosis, and the longest recorded survival was only 4 years (Swenson, 1943).

Lymph-node Involvement. — It is perhaps understandable that most surgeons should equate enlarged mesenteric lymph-nodes in these cases with secondary tumour involvement. Yet many of the enlarged nodes show only follicular hyperplasia and sinus reaction. If the bowel lesion is considered to be a large inoperable carcinoma and a biopsy is taken only from a mesenteric lymph-node the true nature of the bowel lesion may be missed. The surgeon may then be denied the benefit of second thoughts about the operability of the lesion, the only treatment which holds out any real hope of cure for the patient, and the patient may be denied the benefits of radiotherapy. Regional lymph-node involvement was found in 52 per cent of our 37 cases, and it did not appear to have any significant effect upon prognosis. This surprising finding has been noted by others, e.g., Marshall and Meissner (1950), Marcuse and Stout (1950), Allen and others (1954), and Azzopardi and Menzies (1960).

Influence of Cell Type.—We were unable to find any record of benign Hodgkin's disease (paragranuloma) affecting the gastro-intestinal tract, nor any record of a primary giant follicular lymphoma of the stomach. Nearly all the tumours in young children were lymphosarcomas, and reticulum-cell sarcoma, Hodgkin's disease, and Hodgkin's sarcoma were all found in an older age-group.

Some writers have found that in cases of primary malignant lymphoid tumours of the gastro-intestinal tract there appeared to be no significant relationship between cell type and survival (Warren and Lulenski, 1942; Usher and Dixon, 1943; Faulkner and Dockerty, 1952; and Irvine and Johnstone, 1955). Marcuse and Stout (1950), Skrimshire (1955), and Azzopardi and Menzies (1960) have noticed that primary giant follicular lymphomas have a better prognosis than the other primary malignant lymphomas. Allen and others (1954) noticed that primary reticulum-cell sarcoma, lymphoblastic lymphosarcoma, and Hodgkin's sarcoma appeared to have a worse prognosis than primary giant follicular lymphoma, lymphocytic lymphosarcoma, and Hodgkin's disease. Raiford (1932) and Spellberg and Zivin (1949) noticed that primary reticulum-cell sarcomas had a poorer prognosis than the primary lymphosarcomas. Until more primary cases surviving the 5-year and 10-year periods are on record it will not be possible to come to any definite conclusion, but our survey tends to suggest that there is a relationship between cell type and length of survival. Giant follicular lymphomas appear to have the best prognosis, and lymphosarcomas appear to have a better prognosis than reticulum-cell sarcomas, Hodgkin's disease, and Hodgkin's sarcoma.

Associated Diseases.—Primary malignant lymphomas of the colon are uncommon and the finding of malignant lymphomas complicating 7 cases of chronic ulcerative colitis (Cornes, Smith, and Southwood, 1961) may have some significance; a relationship between these two disorders cannot be excluded. Too few cases have been reported to assess the influence of ulcerative colitis on length of survival. However, of the 7 cases recorded, 4 died within 18 months, 2 were alive and had local recurrences within 9 months of surgical resections, and only 1 patient was reported alive and well 1 year after operation.

Four of our 37 intestinal cases were associated with carcinomas, 3 of which were primary carcinomas in the colon or rectum. Very few cases of this type have been described (Cornes, 1960). These unusual findings underline the importance of an adequate clinical follow-up on all cases, and urge caution against assuming that a second growth in the intestinal tract is necessarily a recurrence or a metastasis from the original primary tumour.

Treatment.—Some authors regard 5-year survivals after treatment as cures or apparent cures. But there are several reports of patients developing a local recurrence or a generalized spread of their disease, and dying in the 5–10-year period. We have found no report of any patient with a primary intestinal lesion surviving more than 10 years with evidence of recurrent disease, and none of the deaths in patients who lived for 10 years or more after operation were related to their original disease. For these reasons we think it wise to regard only 10-year survivals as apparent cures.

All the patients with a primary intestinal lesion who lived for 10 years from the time of diagnosis had been treated by surgery, or by a combination of surgery and radiotherapy, and there is general agreement that a wide surgical removal of the intestinal lesion together with the neighbouring lymph-nodes is the treatment of choice. A striking feature of some of these lesions is their large size, and this alone should not deter a surgeon from attempting a surgical removal. There are several reports of cases at first thought to have been inoperable because of the size of the bowel lesion, which survived for many years after operation. The triad of a large tumour of the bowel with a short clinical history, and a striking lack of emaciation, should suggest the diagnosis of malignant lymphoid tumour rather than carcinoma. Large carcinomas are usually necrotic, and are often associated with severe emaciation, toxic symptoms, metastases, and a bad prognosis.

A few cases similar to the third case in our series have been described in which the tumours were multiple, or involved fairly long segments of the bowel, and prevented their complete surgical removal. Despite incomplete removal, some of these intestinal cases survived several years, some with and some without post-operative radiotherapy (Allen and others, 1954). Similar results have been reported in the gastric cases (Pattison, 1934; Stout, 1953; Thorbjarnarson and others, 1959).

There is general agreement that radiotherapy should be used in inoperable cases, in cases with regional lymph-node involvement, and in those cases in which tumour is found at the resected end of an operation specimen. The value of post-operative radiotherapy in cases in which the bowel lesions have been completely removed and the regional lymph-nodes are not involved is still a matter for dispute. Several cases surviving the 10-year period have been treated by surgery alone, so post-operative radiotherapy is not essential for a long survival. We could find no compelling data for or against radiotherapy in such cases. In those cases shown to be associated with a bad prognosis (lymphoblastic lymphosarcoma, reticulum-cell sarcoma, Hodgkin's disease, and Hodgkin's sarcoma), a prophylactic, post-operative course of radiotherapy would appear to be a wise procedure.

A striking feature of all reported series of malignant lymphoid tumours of the intestinal tract is the high percentage of deaths occurring in the first two years from the time of diagnosis or treatment. This is partly accounted for by post-operative deaths, and partly by the fact that quite a number of the recorded cases may not have been primary bowel tumours. In some cases it is possible that the bowel lesions were only the earliest manifestation of a generalized disease, and were noticed before the more distant lesions became obvious.

In any study of malignant lymphoid tumours there are always 2–3 per cent of the cases which show a long survival irrespective of the extent of lymph-node involvement, or of treatment (Stout, 1942). We have already drawn attention to the records of long survivals after the incomplete removal of some malignant intestinal lymphomas. The fact that some patients have been complaining of symptoms for four or five years before they were first seen further suggests that some tumours can remain localized for long periods of time before spreading to other parts of the body. Why some tumours remain localized for such long periods of time has never been fully explained, and there is still much to be learnt about the behaviour of these tumours and the best methods of treating them.

SUMMARY

1. Thirty-seven cases of malignant lymphoid tumour primarily situated in the intestinal tract are described.

2. Strict criteria are suggested for separating primary bowel lesions from other malignant lymphomas and for distinguishing between benign lymphoid polyps and malignant lymphomas of the rectum.

3. Small-bowel tumours most commonly present with symptoms suggesting an obstructive lesion. Large-bowel tumours present with altered bowel habits and melæna. In roughly a third of all cases the only complaints are malaise and vague pains, until the sudden onset of obstruction or perforation brings the patient into hospital.

4. Four types of intestinal tumours can be found: annular, or plaque-like lesions; bulky and protuberant growths; aneurysmal bowel lesions; and multiple lymphomatous polyps spread over long segments of the intestinal tract.

5. A few of the intestinal lymphomas are associated with carcinomas, either at the time of operation or developing after the intestinal lesion has been removed.

6. No case surviving 10 years had evidence of recurrent disease or died from the original disease. Cases surviving the 5-year period can develop recurrences, and may die from the original disease in the 5–10-year period. Only 10-year survivals should be regarded as apparent cures. When strict criteria are used to diagnose a primary lesion there is no evidence that age, sex, or the number of tumours found have any significant effect upon prognosis.

7. All the adequately recorded cases said to have survived 10 years were treated by surgery, or by combined surgery and radiotherapy, and no case treated solely by radiotherapy survived for 10 years. We were unable to show that radiotherapy significantly lengthened a patient's chance of survival.

8. Lesions in the stomach have a better prognosis than similar lesions in the intestinal tract; duodenal lesions have a worse prognosis.

9. Giant follicular lymphoma and lymphosarcoma have a better prognosis than reticulum-cell sarcoma, Hodgkin's disease, or Hodgkin's sarcoma.

10. We were unable to show a relationship between prognosis and regional lymph-node involvement.

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REVIEWS OF BOOKS

Additional Reviewers are required for books in foreign languages other than French and German, particularly Spanish. Such books would become the property of the Reviewer. Surgeons interested should communicate with the Editorial Secretary.

DIABETIC ACIDOSIS WITH ACUTE PANCREATITIS

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DIABETIC acidosis with acute pancreatitis is a long-recognized but little publicized condition. The first recorded case was that reported by Benda and Stadelmann in 1896, occurring in a previously symptomless 23-year-old woman. In 1924 Holten reported the first case of this kind in which insulin was used in treatment. I have been able to find a total of 57 cases previously reported in the literature (39 of them being in known diabetics), to which another case is added. Acute pancreatitis may precipitate diabetic acidosis in the known diabetic or in non-diabetic patients known to have had sugar-free urine shortly before the attack of pancreatitis. This diabetes may then persist as permanent diabetes mellitus after recovery from the acute pancreatitis.

CASE REPORT

A 76-year-old obese female was admitted to St. John's Hospital, Lewisham, on May 7, 1959, complaining of severe abdominal pain for 24 hours. The patient was a mild diabetic, who had been well controlled on diet and oral tolbutamide (rastinon) tablets 0·5 g. twice daily.

The pain had come on suddenly, was severe and persistent, and vaguely localized in the upper abdomen. There was no radiation to the back. There had been occasional vomiting, slight in amount. The patient had passed no flatus from the time of commencement of the pain. There had been no previous attacks of similar pain.

ON EXAMINATION.—The patient was dehydrated and mildly delirious, but not comatose. The temperature was 97·0° F. The pulse-rate was 125 per min., and the respiration rate 24 per min. There was acute generalized abdominal tenderness, with guarding and rebound tenderness, which was most marked in the upper abdomen. There was no tenderness in the renal angles, and rectal examination revealed no abnormality. Auscultation of the abdomen, up to 3 min., revealed no bowel-sounds.

The blood-pressure was 160/90 mm. Hg, and no abnormality was detected on clinical examination of the respiratory or cardiovascular systems. The urine was macroscopically clear, with a specific gravity of 1·026. Ward testing showed sugar ++++, and acetone +++.

A diagnosis of diabetic acidosis, with associated abdominal symptoms, was made, and treatment instituted along the lines laid down by Nabarro, Spencer, and Stowers (1952). Soluble insulin, 20 units intravenously and 40 units intramuscularly, was given. An intravenous drip was started, and normal (0·9 per cent) saline run in rapidly.

Blood-sugar was found to be 670 mg. per cent. Serum electrolyte estimations showed bicarbonate 15·6 mEq./l., potassium 5·5 mEq./l., sodium 132 mEq./l., chloride 102 mEq./l., and urea 80 mg. per cent.

1500 ml. of normal saline, and 1500 ml. of 1/6 M. sodium lactate were given in 4 hours. At the end of this time urine testing showed sugar +, and a trace of acetone. Blood-sugar was 240 mg. per cent, serum bicarbonate 27·5 mEq./l., and potassium 4·1 mEq./l.

The abdominal signs were slightly diminished, but still marked, and the pulse-rate was 130 per min. A provisional diagnosis of perforated peptic ulcer was made and laparotomy decided upon. The intravenous infusion was changed to 5 per cent dextrose, and a further 15 units of soluble insulin were given intramuscularly.

AT OPERATION.—Laparotomy was performed under general anæsthesia. The peritoneal cavity contained 1 litre of lightly blood-stained fluid. There were white patches of fat necrosis scattered over the omentum. The gastro-colic ligament was opened, and the pancreas found to be grossly swollen, with areas of hæmorrhage on its surface. The gall-bladder contained no stones; the common bile-duct was not dilated, and was normal to palpation. The abdomen was closed without drainage.

After operation, the patient had paralytic ileus for 9 days. This was treated by gastric aspiration through a Ryle's tube and intravenous fluids. 600 calories of carbohydrate daily were supplied as 3 litres of 5 per cent glucose in 0·18 per cent saline. 50 mEq. of potassium as potassium chloride were given in the intravenous fluids on alternate days. Soluble insulin was given to scale on 4-hourly urine testing. This régime maintained satisfactory fluid and electrolyte balance, and control of the diabetes.

The ileus subsided, and the patient was gradually able to return to her usual diet. Her bowels were acting satisfactorily. After a further five days the patient developed acute dilatation of the stomach. This was treated by gastric suction and an intravenous régime as above. This also gradually subsided, and the patient started to take small amounts of diet once again. Her general condition started to deteriorate, and a clinical diagnosis of left basal pneumonia was made. This was treated with penicillin and streptomycin, but the patient died, one month after admission.

Post-mortem examination showed bilateral basal bronchopneumonia, and acute pancreatitis, with an abscess of the body of the pancreas. There were no stones in the common bile-duct.

This case prompted a search of the literature for any association between acute pancreatitis and diabetes mellitus. In 1862 Harley reported glycosuria in a patient with an abscess of the pancreas. Schumaker (1940) found glycosuria in 11 per cent of 700 collected cases of acute pancreatitis. Brocq and Varangot (1937) found the fasting blood-sugar to be over 200 mg. per cent in 34 out of 72 cases of acute pancreatitis in which blood-sugar estimations had been made. This was usually transient.

I found 7 cases (Albu, 1911; Bernhard, 1931; Matthaes, 1931; Peisner, 1902; Schumaker, 1940; Warren, Fallis, and Barron, 1950) of patients who were known to have sugar-free urine either shortly before, or at the beginning of, an attack of acute pancreatitis, who developed diabetes during the attack (2 had acidosis), and which persisted as permanent diabetes mellitus after the pancreatitis had subsided.

Fourteen cases are recorded (Albu, 1911; Bayer, 1930; Caldwell, 1954; Holten, 1924; Rodriguez, 1924; Rose, 1951; Smith, 1942; Tscherning, 1925; Vallance-Owen, 1960; Warfield, 1927; Warren, Fallis, and Barron, 1950) of patients who were known to have sugar-free urine before or at the beginning of an attack of acute pancreatitis, and developed diabetic acidosis or coma during the attack. Only 3 of these survived, 2 with permanent diabetes mellitus (included in the group of 7 above). Another 4 cases (Benda and Stadelmann, 1896; Franke, 1902; Neumann, 1904; Tully and Lowentha!, 1958) who had no previous symptoms and were presumably not diabetics, developed diabetic acidosis or coma during an attack of acute pancreatitis. All 4 died. There were thus 3 survivors out of 18 cases of non-diabetics who developed diabetic acidosis during an attack of acute pancreatitis.

There are 28 cases recorded (Beck, 1937; Cabot, 1930; Cullen and Friedenwald, 1927; Douglas, 1933; Felsenreich, 1932; Foord and Bowen, 1930; Jacobovici, 1933; Joslin, 1937; Lawrence, 1960; Schott, 1926; Schufftan, 1927;

Schumaker, 1940; Steiner and Tracy, 1943; Truesdale, 1934; Tully and Lowenthal, 1958; Unger and Sostmann, 1931; Vogel, 1924; Warren, 1927) of diabetic acidosis with acute pancreatitis in known diabetics. There were 2 survivors out of the 20 cases in which the outcome is stated.

The apparently high mortality is partly offset by the fact that acute pancreatitis in such cases is usually not suspected unless severe enough to cause death or provoke operation. Rose (1951) reported 3 cases of diabetics who had survived an attack of acute pancreatitis.

Out of 102 cases of death in resistant diabetic coma, the main pathology found at post-mortem examination was acute pancreatitis in 11 cases (Bowers and Atkins, 1942; Root, 1937; Rose, 1951). This was usually unsuspected during life. These 11 make 39 cases of diabetic acidosis with acute pancreatitis in diabetics. Adding the 18 cases in non-diabetics makes a total of 57 cases.

DISCUSSION

It is well recognized that abdominal signs and symptoms may occur with diabetic acidosis, without any apparent pathological basis, even with a white-cell count of 50,000 per c.mm. (Lawrence, 1960b). It is highly likely that a large proportion, but certainly not all, of the cases of abdominal pain associated with diabetic acidosis are due to a mild attack of pancreatitis which settles down and is not recognized. Serum-amylase estimations on every case of diabetic acidosis will provide further information on this.

It has been shown that disturbances of carbohydrate metabolism are not uncommon during an attack of acute pancreatitis, and that permanent diabetes mellitus may result. Blood-sugar studies on every case of acute pancreatitis will throw more light on this. There is nothing surprising in the fact that diabetes mellitus may be diagnosed for the first time during an attack of acute pancreatitis. Pneumonia or any other stress may precipitate diabetes in a potential diabetic. However, the fact that many of these cases went promptly into diabetic acidosis is much more significant. Out of the 23 cases of non-diabetics which developed diabetes during an attack of acute pancreatitis, 18 went into acidosis, with a mortality of 83 per cent. This points to a much more specific significance of the acute pancreatitis.

CONCLUSIONS

1. Acute pancreatitis occasionally causes diabetes mellitus, which is then often fulminating.

2. Acute pancreatitis is sometimes the underlying cause of resistant diabetic coma.

3. Acute pancreatitis is the underlying cause of a yet undetermined proportion of the abdominal signs and symptoms that are sometimes associated with diabetic acidosis.

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MULTIFOCAL OSTEOGENIC SARCOMA

A CASE REPORT

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MULTIFOCAL osteosarcoma is uncommon; its occurrence in patients not known to be affected by some recognized predisposing factor such as Paget's disease or the ingestion of long-life, bone-seeking radioactive materials is rare. Some confusion with primary bone tumours metastasizing to bone occurs, but low-grade, primary, multifocal osteosarcoma occurring in middle age appears to be a distinct entity. We submitted a brief account of this patient before her death, together with radiographs and histological sections, to the Eleventh Cancer Seminar at Colorado Springs on the request of Dr. J. A. del Regato when it was reviewed by the panel (1959). Several diagnoses were proposed by the pathologists attending, amongst which was melorheostosis, which it clearly was not; no one present was familiar with this condition, though the majority favoured a histological diagnosis of low-grade osteosarcoma. So few of these patients have been reported that an additional case with an account of the post-mortem examination which is now available seems well worth recording.

FIG. 96.—Extensive osteoblastic tumour of the right femur.

FIG. 97.—Dense osteosarcoma of the sacrum.

FIG. 98.—Osteosarcoma of the left humerus.

CASE REPORT

CLINICAL SUMMARY.—E. M. (029613), a woman of 51 years of age when first seen by us in 1956, complained of pain in the right thigh for eight months, starting at the menopause. Radiographs showed the appearance of multiple osteogenic sarcomata with involvement in the upper and middle thirds of the right femur (*Fig.* 96), the lower end of the right femur, the pelvis (*Fig.* 97), the sacrum, the lumbar spine, and in the left humerus (*Fig.* 98). The lungs appeared normal. Pieces were

removed for biopsy from four separate areas: the cortex of the right femur, the medulla of the right femur, the posterior iliac spine, and the sacrum. All showed identical histological appearances and were reported as osteogenic sarcoma. All these lesions were present when the patient was first examined. Her general condition was excellent; she was working in charge of a group of addressograph operators; her only complaint was pain in the right thigh; she was unaware of the presence of the other lesions.

INVESTIGATIONS.—

White blood-cells: 3200 per c.mm. Differential count normal. Hæmoglobin 78 per cent. Platelets 134,000 per c.mm.

Urine calcium: Sulkowitch's test: + ve (1 +).
Serum-calcium: 9·1 mg./100 ml.
Serum-phosphorus: 3·4 mg./100 ml.
Serum-acid phosphatase: 4·0 units/100 ml.
Serum-alkaline phosphatase: 25·4 units/100 ml.

At a later date:—

Serum-calcium: 10·9 mg./100 ml.
Serum-phosphorus: 4·2 mg./100 ml.
Serum-alkaline phosphatase: 23·0 mg./100 ml.
Serum-bilirubin: total, 0·5 mg./100 ml.
Serum-protein: total, 7·3 g./100 ml.; albumin, 4·9 g./100 ml.; globulin, 2·3 g./100 ml.
A/G ratio: 2·2 : 1.
Serum paper electrophoresis: within normal limits.
Serum thymol turbidity: 2 units.
Serum thymol flocculation: 1 +.
Serum zinc sulphate turbidity: 6 units.
Serum ammon. sulphate turbidity: 3 units.
Colloidal gold reaction: 0.
Blood-urea: 24 mg./100 ml.
Plasma-electrolytes: normal.

Insulin sensitivity: normal, indicating no excess of somatotrophic growth or diabetogenic hormone.

Urine calcium: 15·1 mg./100 ml. or 0·6 g. in 31 hr.
Urine phosphorus: 40·7 mg./100 ml. or 1·5 g. in 31 hr.
Urine creatinine: 43·0 mg./100 ml. or 1·3 g. in 31 hr.
Phosphorus clearance: 21·5 ml. plasma per min.
Creatinine clearance: 95·0 ml. plasma per min.
Phosphate excretion index: +0·04.

There was no evidence of excessive parathyroid activity.

17-ketosteroids: 8·1 mg./day (volume of 48 hr. specimen of urine = 4500 ml.).

Radio-active calcium studies were carried out in October, 1956, and in January, 1958: 30 μc. was given on the first occasion and 50 μc. on the second. These detailed studies are of interest, suggesting that the plasma clearance curve may be composed of three exponentials with half times of 392 min., 21 min., and 4·5 min., representing excretion, bone deposition, and exchange in equilibrium with extracellular fluid respectively.

PROGRESS.—She was treated locally by X rays to the painful areas for relief of pain and generally by giving radio-active phosphorus (P^{32}) and androstalone. The first course of treatment was given in October, 1956, when she had 1 mc. of P^{32} at a time on fifteen occasions between Oct. 26 and Nov. 15, 1956; she received an injection of 15 mg. of androstalone on each occasion with the P^{32}. Local X-ray treatment was given, in doses of 1500–2000 r at a time, in short courses to the painful areas. Relief was quickly obtained on each occasion by this method. The P^{32} course was repeated in January, 1957, with oral testosterone, a further 15 mc. of P^{32} being given between Jan. 21 and Feb. 8, 1957. Following the second course of treatment she had a delayed drop in her blood-count and a low platelet count with some bruising relieved by a blood transfusion, following which her blood-count recovered.

After treatment there were definite changes in the X-ray appearances of some of her multiple tumours; the tumour on the left side of the sacrum became considerably smaller and the one on the right became less dense. Some improvement appeared around the base of the humeral head on the left side. A new tumour appeared

FIG. 99.—Longitudinal section of the right femur, showing extensive involvement by sclerosing osteosarcoma.

in the left ischium, however, and there was less sclerosis of the body of the 2nd lumbar vertebra, with more bone destruction. Until the middle of 1959 she remained in good health and for most of the time she was free enough of pain to be able to do her work. In July, 1959, however, she quickly became weak and anæmic, her hæmoglobin fell to 55 per cent, she was admitted to hospital, and blood transfusions were given, but she developed a respiratory tract infection and died on Aug. 20 three years after first reporting to us. Her hæmatopoietic failure may have been due to the combination of P^{32} and bone-marrow destruction by the tumours.

SUMMARY OF POST-MORTEM FINDINGS.—

External appearances: The body appeared adequately nourished. There were no skin lesions. No jaundice or œdema was present.

Cardiovascular system: No significant changes.

Respiratory system: There was confluent broncho-pneumonic consolidation of the right upper and middle lobes and the upper half of the right lower lobe; the left upper and lower lobes showed discrete foci of broncho-pneumonia.

Alimentary system: The liver was enlarged and pale (weight 2638 g.). There were no focal lesions to be seen macroscopically.

Genito-urinary system: The uterus contained an intramural fibroid, 6 cm. in diameter; there were no other changes. The *spleen* was enlarged (weight 937 g.). Its cut surface was deep red in colour; the grey Malpighian bodies could still be seen.

Bone-marrow: The sternal and vertebral marrow (apart from the tumour areas) was a homogenous pink colour.

C.N.S.: No macroscopic changes.

Skeletal system: Almost the whole of the right femur, except for part of the head and lower condyles, showed a striking overgrowth of white sclerotic bone which formed irregular projections on the external surface, effaced the distinction between the cortex and the spongiosa, and almost obliterated the medullary cavity (*Fig.* 99). The body of the 2nd lumbar vertebra was completely replaced by similar sclerotic bone (*Fig.* 100). The diameter of the vertebra was increased by 3–4 cm., but its thickness was little different from normal. The sacrum, the left ischium,

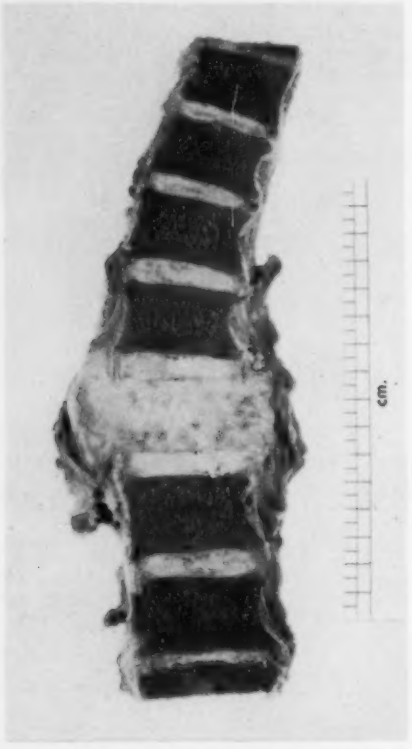

FIG. 100.—The body of the 2nd lumbar vertebra is completely replaced by sclerosing osteosarcoma.

and the left humerus were affected by a similar process. The disease involved the lower part of the head of the humerus and the upper 10 cm. of the shaft, including the medullary cavity (*Fig.* 101). An apparently separate focus of early tumour formation was seen in the cortex 3 cm. above the lower end; the focus consisted of slight thickening and increased density of the compact bone. All the other bones examined appeared normal. In particular there was no evidence of any underlying precancerous abnormality (such as Paget's disease).

Histology.—By the time of the patient's death most of the tumour tissue had been transformed into dense neoplastic bone which showed extensive necrosis (*Fig.* 102). However, at the periphery of the lesions it was possible to find actively proliferating, cellular growth composed of irregular tumour osteoblasts (*Fig.* 103). These cells showed only a few mitotic figures, but there were some abnormal forms. Osteoid production was abundant in such areas and all transitions could be seen to the inactive sclerotic bone. The microscopical appearances were considered to be those of slowly growing, sclerosing osteosarcomata of low-grade malignancy.

DISCUSSION

Multiple osteosarcomatous masses in the skeleton may result from either (1) metastases from a single primary or (2) multicentric tumour formation.

Metastatic spread of an osteosarcoma to other bones is a rare event. Willis (1952) cites 12 cases of bone sarcoma (of various types) disseminating to other parts of the skeleton. Lichtenstein (1952a) simply states that "on occasions one may observe late metastases in one or more of the other bones".

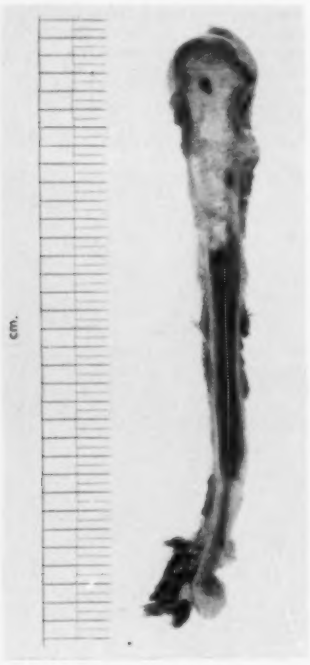

FIG. 101.—Longitudinal section of the left humerus. Sclerosing osteosarcoma involves the upper 10 cm. of the shaft.

Similarly, Jaffe (1958a) remarks "occasionally one or more skeletal metastases are observed . . . if foci of skeletal metastases do appear, they are most likely to be found in the vertebral column, the skull and/or the pelvic bones". Finlayson (1953) reported the case of a 12-year-old girl who had an osteogenic sarcoma of the left ulna. The arm was amputated above the elbow, but she died about 17 months later. At necropsy there were tumour deposits in the scapulæ, pelvic bones, right humerus, ulna, and radius, both femora, both tibiæ, both patellæ, skull, vertebræ, ribs, and right clavicle. Metastases were also present in both lungs. Finlayson reviewed the previous records of osteogenic sarcoma involving more than one bone and concluded that "multiple skeletal metastases from a primary bone tumour

rather than multicentric osteogenic sarcomatosis offer a reasonable explanation of at least the majority of cases". We have seen a few metastases from bone to bone; one remarkable case of ours was reported by Cohen (1958) in a man aged 59 years (028558) without signs of Paget's disease with an osteogenic sarcoma of the right femur who died with multiple metastases in adrenals, pericardium, lung, and in both rami of the mandible.

Multicentric tumour formation in bones affected by Paget's disease is well recognized (Derman, Pizzolato, and Ziskind, 1951; Lichtenstein, 1952a; Jaffe, 1958b), and multiple independent osteosarcomata have also been reported after chronic exposure to radiation in luminous-dial painters (Martland, 1931). In the absence of such predisposing factors, however, multicentric osteosarcomata are rare. Silverman (1936) reported the case of a 27-year-old man in whom multiple bone tumours apparently developed synchronously in the skull, sternum, ribs, scapula, vertebræ, pelvis, and humerus, but there were metastases in the lungs and pericardium. Lichtenstein (1952b) refers briefly to 2 cases of osteosarcoma developing in multicentric foci, and Jaffe (1958a) comments on the intense radiopacity of the tumours in the reported cases. Ackerman (1948) reported 2 cases. Busso and Schajowicz (1946) reported an example in an 8-year-old child. Moseley and Bass (1956) recorded the case of a girl aged 5 years who had sclerosing osteogenic sarcomatosis but no pulmonary metastases. The patient of Rowen (1955) was a 36-year-old man who developed sclerosing osteosarcomata in both femora and was of further interest because the patient's elder brother had died from a sarcoma of the femur. Price and Truscott (1957) reported a case much more closely resembling our own: a woman aged 50 years who had widely distributed ossifying skeletal tumours without visceral metastases. In many of these cases there seems to be some doubt whether true multifocal origin in different bones occurred or whether metastases from one bone to others could account for the condition found.

Primary osteogenic sarcomas occur predominantly in patients who are either under 35 years of age or over 50 years (Price, 1955). In the younger age-group the males predominate but the females tend to get their tumours earlier (maximum incidence 5–14 years for girls and a decade later for boys) corresponding to the time of the adolescent growth spurt. The greater total tumour incidence in boys may be due to the relatively increased growth in length of their bones, with a greater bulk of tissue involved in the growth stimulus for a longer time. The highest site incidence corresponds to the regions of maximal growth in length. In the older age-group males predominate again; one-half of these cases are associated with Paget's disease (where the sex incidence is approximately equal) and some of the others with osteoclastomas, enchondromas, or advanced osteoporosis. The intermediate age-group provides too few cases for detailed study. There appears at present, however, to be a female preponderance here and a possibility of a menopausal relationship. In girls the adolescent growth spurt is related to the time of the menarche. Sex hormones have a marked influence on bone growth and the difference in sex incidence between patients with fibrosarcomas and osteogenic sarcomas suggests an influence in the bone tumours of some factor which is sex hormone-dependent. The case reported here and that of Price and Truscott (1957) are very similar and further records of cases of multifocal osteosarcoma in middle age would be of great interest.

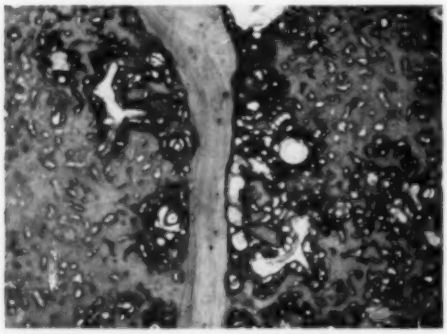

FIG. 102.—Photomicrograph of irradiated area, showing dead tumour bone surrounding an original trabecula. H. and E. (× 43.)

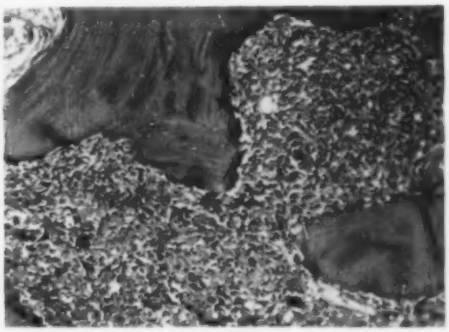

FIG. 103.—Photomicrograph of cellular area showing osteosarcomatous tissue infiltrating between the original trabeculæ of the bone. H. and E. (× 43.)

SUMMARY

The details of the history, treatment, and post-mortem findings in a woman of 51 years of age who developed widespread low-grade, multifocal osteosarcoma are given. The comparative rarity of primary bone tumours at this age, particularly in the absence of Paget's disease, is stressed, together with the many similarities between this case and the one published by Price and Truscott (1957), including diagnosis at the time of the menopause.

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EXPERIMENTAL SURGERY

WOUND CONTRACTION IN THE GUINEA-PIG

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WOUND contraction has been widely recognized as a major factor in the repair of full-thickness excised skin wounds in common laboratory animals. The term 'wound contraction' describes the centripetal movement of the intact skin bordering the deficit during the early stages of repair. As its consequence, the end-product of wounding is a scar of substantially smaller area than the deficiency evoking it. In the rabbit, for example, a skin wound some 6 cm.^{2} in initial area may be reduced by the twelfth post-operative day to a fifth of its original size (Abercrombie, James, and Newcombe, 1960). While the skin surrounding the wound is initially stretched by the contraction process, and consequently thinned, its thickness is later restored by a process of intussusceptive growth (Billingham and Medawar, 1955; James, 1959).

The relationship between wound contraction and the clinically more familiar 'contracture' is obscure. The latter term, however, is perhaps best reserved to describe the shortening or reorientation of an established mass of scar tissue. It is clear that the two processes, 'contraction' and 'contracture', are at least distinct in time. There can be little doubt that wound contraction occurs in man. It was in fact clearly described by John Hunter (1792), and is encountered in current practice, for example, when the wound resulting from the wide excision of an anal fistula is encouraged to granulate from its floor. While only recently (Dunphy, 1960) has clinical trial of the potentialities of wound contraction in a variety of sites been suggested, its mechanism is of obvious importance for the understanding of the repair process in excised wounds.

Unfortunately, experimental investigations of the mechanism of wound contraction have led to no generally agreed conclusion. The 'classical' hypothesis—that contraction is in some way mediated by newly formed collagen laid down within the wound—appears untenable in view of the observation that in scorbutic animals, in whose wounds no collagen is laid down, the course of contraction conforms in both time and extent with contraction in non-scorbutic animals (Abercrombie, Flint, and James, 1956; Grillo and Gross, 1959). Watts, Grillo, and Gross (1958) attributed contraction in the guinea-pig to the activity of a zone of cells beneath the wound margins. These cells, they believed, migrated centripetally and carried the wound edges with them as they did so—the 'picture frame' hypothesis. Watts and his colleagues denied that the granulation tissue mass was itself contractile, since an island of granulation tissue freed from its peripheral attachments by a suitable incision did not contract. Neither, in their view, did such incision lead to retraction of the surrounding skin margin, as would be expected if the granulation tissue mass were exerting a centripetal force upon the wound edges, working against the normal tension of the skin.

These findings, however, conflicted with those of previous investigators. In the rat, Lindquist (1946) found that when the granulation tissue within a skin wound was freed from the skin margins by incision, it contracted. Abercrombie, Flint, and James (1954) confirmed this observation, and noted that under such circumstances granulation tissue contraction was associated with a consistent retraction (i.e., movement away from the wound centre) of the surrounding skin margins.

Abercrombie and others (1960) reinvestigated the problem in rabbits. They worked with wounds whose contraction was first impeded by a splinting technique, and later released, and concluded that granulation tissue was not only contractile, but contracted sufficiently strongly to account for the inward movement of the skin margins.

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Before any general hypothesis of contraction can be put forward, it is clearly necessary to decide whether such major divergencies of opinion as those summarized above reflect differences in the contraction mechanism in the guinea-pig on the one hand, and in the rabbit and rat on the other, i.e., are attributable simply to species difference.

We thus thought it of interest to apply to the guinea-pig the techniques for the study of contraction used by Abercrombie and others (1960) in the rabbit. We have consequently investigated in the guinea-pig the rapid and marked wound contraction that follows release from splinting. We have also investigated the effects of this rapid contraction upon the composition and weight of standard areas of granulation tissue defined by tattooing within the wound before contraction was permitted.

Our findings reveal no evidence for a contraction mechanism unique to the guinea-pig. On the contrary, they suggest that in the guinea-pig contraction is largely comparable, both in pattern and in effect on the granulation tissue within the wound, with contraction in the rabbit or rat.

MATERIAL AND METHOD

Results are reported from 33 male white guinea-pigs from breeders' stock (mean body-weight 618 g., range 420–875 g., standard error 93). Animals were anæsthetized with intraperitoneal pentobarbitone (nembutal), 30 mg./kg. body-weight, reinforced when necessary with open ethyl ether. The sides of the thorax were clipped with electric clippers, and depilation completed by wet shaving.

A 2 × 2 cm. square was marked on the chest wall by Indian ink dots defining its corners and the midpoints of its sides. These were parallel to the craniocaudal and dorso-ventral axes of the animal. Each of the dots was then tattooed by pushing through it a 2 cm. straight cutting needle loaded with Indian ink and rotated before withdrawal. In this way both epidermis and dermis were simultaneously tattooed. The tattoos were traced on to cellophane, and the square they enclosed was aseptically excised. Both skin and panniculus carnosus were removed, and tattoos were left intact to mark the wound margin. Excised tissue was placed in a stoppered bottle for subsequent weighing. A 4 × 4 cm. square of $\frac{1}{16}$-in. thick perspex was then bent to approximate conformity with the thoracic wall, and a central square aperture, 2·5 × 2·5 cm., cut in it. The wound margins were manipulated to lie just within the aperture and the splint was glued to the skin surrounding the wound with Eastman's 910 adhesive. Tattoo marks were again traced on to cellophane, and the wound sprayed with sulphathiazole/penicillin powder. It was dressed with carbonet (Smith & Nephew) and gauze. The whole procedure was repeated on the contralateral side, and the dressings held in position with encircling crêpe bandage and zinc oxide adhesive tape.

On the tenth post-operative day animals were re-anæsthetized with ethyl ether and their dressings removed. Obvious loosening of a splint or infection of a wound led to rejection at this stage. In animals satisfactory in these respects a 1 × 1 cm. square marked by a dot at each corner was tattooed centrally on the granulation tissue within each wound, its sides parallel to the wound margins. Up to this point, the splints in all cases remained undisturbed, and the skin and granulation tissue tattoos were traced on to cellophane. *Fig.* 104 illustrates the procedure diagrammatically.

Wounds were subsequently treated in one of three ways: In the first (Treatment A) the square of granulation tissue delimited by tattoos was isolated by straight incisions along its edges (*see Fig.* 104), carried down to the fascia constituting the wound bed. Ten minutes later a tracing was made of the granulation tissue island, of the granulation tissue margin surrounding it, and of the tattoos marking the borders of the original wound. The splint was undisturbed throughout, and finally the granulation tissue island

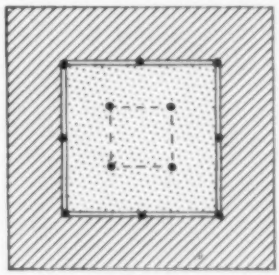

FIG. 104.—After granulation tissue tattooing at 10 days (diagrammatic). Within the splint (cross-hatched) are shown the eight tattoo dots marking the wound margin, the granulation tissue (stippled) and the 1 cm. square demarcated on it by four tattoos. The dotted lines joining these indicate the line of subsequent incision.

was dissected off the wound bed for analysis. In 12 of the wounds thus treated, the splint was removed after granulation tissue biopsy and the wound redressed. Two days later (on the twelfth day) skin tattoos were traced again.

In the second (Treatment B) splints were removed after granulation tissue tattooing on the tenth day. Ten minutes later a further tracing of the tattoos was made, and the wound re-dressed. Any contraction immediately following splint removal was thus assessed, and a further tracing made on the twelfth post-operative day to estimate contraction between the tenth and twelfth days. Biopsy was then performed as described above.

In the third (Treatment C) dressings were replaced and the splint left undisturbed after granulation tissue tattooing on the tenth day. On the twelfth day biopsy was performed as before with the splints still in situ.

Animals were allotted before operation to one of three groups, using a table of random numbers. All members of a given group received the same two of the three possible treatments (A, B, and C, *see above*), each animal receiving one treatment on one side and one on the other. Sides were again allotted at random.

Areas traced on to cellophane were first re-traced on paper of standard thickness. Areas on the latter were cut out, weighed, and the results expressed as cm.^{2} (*see* Hamlyn, 1954).

Chemical Methods.—Tissue excised at biopsy was weighed in stoppered bottles, dried at 102° C. to constant weight, and stored if necessary at −10° C.

Collagen was brought into solution with hot trichloroacetic acid (TCA) (Fitch, Harkness, and Harkness, 1955). Tissue was heated in 5 per cent TCA for 30 min. at 90° C., homogenized with a Potter-Elvehjem type homogenizer, made to volume with 10 per cent TCA, heated for a further 30 min. at 90° C., and made to final volume with 10 per cent TCA. Two 1-ml. aliquots of the homogenate were taken for micro-Kjeldahl estimation of nitrogen (Ma and Zuazaga, 1942). The remaining homogenate was spun for 15 min. at 2500 r.p.m. and two 1-ml. aliquots of the supernatant pipetted off for hydroxyproline estimation. The method used was that of Neuman and Logan (1950), as modified by Martin and Axelrod (1953). Developed colours were read on a Spekker spectrophotometer at 560 mμ, and hydroxyproline concentrations assessed from standard curves. Collagen was measured from hydroxyproline values, using a factor of 7·46. Non-collagen nitrogen (NCN) was estimated by subtracting collagen nitrogen from total nitrogen.

RESULTS

Results are reported in three sections. The first deals with the randomization of our material from operation until granulation tissue tattooing on the tenth post-operative day; the second records area changes in the three types of wound treatment; and the third changes in wet weight and composition of the tissue excised at biopsy attributable to these treatments.

Table I.—Animal Weights, Weight of Skin removed at Initial Operation, and Tattoo Areas before Operation, after Splinting, and on the Tenth Post-operative Day after Granulation Tissue Tattooing

	Animal Weight before Operation	Treatment	Wet Weight of Skin removed at Operation	Skin Tattoo Area before Operation	Skin Tattoo Area with Splint Applied	Skin Tattoo Area, 10 days	Granulation Tissue Tattoo Area at 10 Days
	g.		mg.	cm.²	cm.²	cm.²	cm.²
Group I	643 ± 28	A	715·2 ± 63·3	4·12 ± 0·11	5·33 ± 0·09	4·43 ± 0·12	0·99 ± 0·02
		B	829·6 ± 81·8	4·04 ± 0·13	5·50 ± 0·20	4·40 ± 0·15	1·00 ± 0·02
Group II	600 ± 29	B	693·3 ± 22·7	4·10 ± 0·13	5·23 ± 0·10	4·23 ± 0·23	1·01 ± 0·03
		C	737·3 ± 33·3	4·23 ± 0·09	5·19 ± 0·09	4·21 ± 0·13	1·04 ± 0·03
Group III	608 ± 32	A	705·0 ± 70·1	4·03 ± 0·09	5·40 ± 0·16	4·18 ± 0·17	1·00 ± 0·03
		C	712·8 ± 56·3	4·06 ± 0·12	5·34 ± 0·12	4·29 ± 0·15	1·02 ± 0·04

Treatment A, Biopsy on the 10th day with splint undisturbed.
Treatment B, Splint removed on the 10th day, biopsy on the 12th day.
Treatment C, Biopsied on the 12th day with splint undisturbed.

Table II.—Mean Area Changes (as mm.²) in Treatments A, B, and C, and the Probabilities with which the Means of Such Changes differ from Zero

	Reduction in Granulation Tissue Area following Incision		Reduction in Tattoo Area between the 10th and 12th Days		Immediate Reduction in Tattoo Area following De-splinting	
	Central Island	Periphery	Skin Tattoo	Granulation Tissue Tattoo	Skin Tattoo	Granulation Tissue Tattoo
Treatment A (22 × 10 day splinted wounds)	0·39 ± 0·02 P < ·001	0·45 ± 0·06 P < ·001				
Treatment B (23 wounds de-splinted at 10 days, biopsied at 12 days)	[1] 0·18 ± 0·01 P < ·001	[1] 0·25 ± 0·07 ·01 > P > ·001	* 1·16 ± 0·13 P < ·001	* 0·32 ± 0·03 P < ·001	[2] 0·69 ± 0·08 P < ·001	[2] 0·13 ± 0·05 ·05 > P > ·02
Treatment C (20 × 12 day splinted wounds)	[3] 0·37 ± 0·04 P < ·001	[4] 0·41 ± 0·06 P < ·001	0·37 ± 0·09 P < ·001	0·16 ± 0·03 P < ·001		

[1] 20 wounds. [2] 22 wounds. [3] 19 wounds. [4] 18 wounds.
* The reduction additional to that immediately following de-splinting on the 12th day.

1. Homogeneity of Material up to Granulation Tissue Tattooing.—It is first necessary to establish that our tattooing, operating, and splinting techniques were adequately standardized. Up to the time of granulation tissue tattooing with the splint

in position on the tenth post-operative day, all wounds were treated alike, and results are summarized in *Table I*. The three groups of animals provided six groups of wounds. Analysis of variance performed on these six groups showed that for each parameter recorded in *Table I* variance within groups exceeded that between them, as it did for mean body-weights in the three groups of animals. It appears, therefore, that up to the tenth day our material was adequately randomized, and all wounds may be considered to constitute a single group. Thus for all wounds mean weight of skin removed at operation was $732{\cdot}9 \pm 23{\cdot}6$ mg. Mean area enclosed by the skin tattoos was $4{\cdot}09 \pm 0{\cdot}11$ cm.^{2} before operation, and $5{\cdot}30 \pm 0{\cdot}06$ cm.^{2} when the splint was in position, an obviously significant increase. By the tenth day skin tattoo area was reduced to $4{\cdot}30 \pm 0{\cdot}06$ cm.^{2}, showing that despite splinting some contraction had occurred. Finally, the mean area enclosed by the granulation tissue tattoo made on the tenth day was $1{\cdot}01 \pm 0{\cdot}03$ cm.^{2}.

2. Area Changes in the Three Treatment Groups.—The adequate randomization established above makes it not unreasonable to consider together all wounds receiving a given treatment. It may be taken that unless otherwise stated the changes in area to be described had less than a 5 per cent probability of chance occurrence (i.e., $P<0{\cdot}05$). To avoid overburdening the text the means of the differences between sets of measurements, and the probabilities with which these means differ from zero, have been relegated to *Table II*.

In each of 22 animals one wound was biopsied with its splint in position on the tenth post-operative day (Treatment A). In such wounds isolation of the granulation tissue tattoo area by incision through its periphery produced two obvious effects. First, the central island diminished in area, and second the surrounding tissue itself contracted, retracting away from the island. Mean granulation tissue tattoo area was $0{\cdot}99 \pm 0{\cdot}06$ cm.^{2} before incision, and $0{\cdot}60 \pm 0{\cdot}21$ cm.^{2} 10 min. later. Before incision the granulation tissue periphery (i.e., that part lying between the central granulation tissue tattoos and those defining the wound margin) was $3{\cdot}29 \pm 0{\cdot}98$ cm.^{2}, while afterwards it was $2{\cdot}84 \pm 0{\cdot}10$ cm.^{2}.

In each of 20 animals one wound, its granulation tissue tattooed as usual on the tenth post-operative day, was biopsied on the twelfth day with its splint undisturbed since operation (Treatment C). Despite splinting, however, some contraction occurred between the tenth and twelfth days, affecting both skin and granulation tissue tattoos. The former were reduced in mean area from $4{\cdot}25 \pm 0{\cdot}01$ to $3{\cdot}88 \pm 0{\cdot}15$ cm.^{2} and the latter from $1{\cdot}03 \pm 0{\cdot}02$ to $0{\cdot}87 \pm 0{\cdot}03$ cm.^{2}. At biopsy the pattern of events was comparable with that described above for Treatment A wounds. Island area was reduced by incision to $0{\cdot}52 \pm 0{\cdot}02$ cm.^{2} and granulation tissue lying peripheral to the island diminished in area from $3{\cdot}03 \pm 0{\cdot}15$ to $2{\cdot}62 \pm 0{\cdot}15$ cm.^{2}. (Some tracings were lost, and figures for island contraction and that of the peripheral granulation tissue are based on 19 and 18 animals respectively.)

The last group of wounds, one in each of 23 animals, comprises those from which splints were removed on the tenth day, and biopsy postponed until the twelfth (Treatment B). Some tracings were again lost, and where means are based upon a number other than the expected 23, this will be indicated.

Splint removal on the tenth day led to a marked reduction of both skin and granulation tissue tattoo areas within the next 10 min. For 22 wounds before splint removal, mean skin and granulation tissue tattoo areas were $4{\cdot}33 \pm 0{\cdot}01$ and $1{\cdot}00 \pm 0{\cdot}02$ cm.^{2}. These means, in 20 wounds, were reduced in 10 min. to $3{\cdot}59 \pm 0{\cdot}13$ and $0{\cdot}86 \pm 0{\cdot}02$ cm.^{2}. Following this rapid contraction, areas diminished still further by the twelfth day, when for the whole group of 23 wounds skin and granulation tissue tattoo areas were $2{\cdot}46 \pm 0{\cdot}11$ and $0{\cdot}57 \pm 0{\cdot}09$ cm.^{2} respectively.

Despite this considerable contraction, area changes at biopsy resembled those already described for continuously splinted wounds. The demarcated central granulation tissue area, $0{\cdot}57 \pm 0{\cdot}09$ cm.^{2} before incision, contracted following it to $0{\cdot}39 \pm 0{\cdot}07$ cm.^{2}. Granulation tissue periphery, $1{\cdot}86 \pm 0{\cdot}07$ cm.^{2} before, was $1{\cdot}61 \pm 0{\cdot}06$ cm.^{2} after incision.

In wounds de-splinted at 10 days and biopsied on the twelfth day the skin margins were not fixed by splints at biopsy, and granulation tissue incision resulted not only in the events described above, but also in an outward movement of the skin bordering the wound. Results are available from 22 wounds, whose mean skin tattoo area was $2{\cdot}43 \pm 0{\cdot}09$ cm.^{2} before the central part of the granulation tissue was separated by incision from its surroundings, and $2{\cdot}56 \pm 0{\cdot}09$ cm.^{2} afterwards. The increase, while small, was consistent ($0{\cdot}13 \pm 0{\cdot}04$ cm.^{2}, $0{\cdot}02>P>0{\cdot}01$).

The final area data to be reported concern the effect of excision of the central tattooed part of the granulation tissue upon the subsequent contraction of the wound. Twelve animals received Treatment A (biopsy at 10 days with splints in situ) on one side and Treatment B (splints removed at 10 days, biopsy at 12) on the other. After Treatment A biopsy at 10 days, however, in these animals splints were removed, and wounds traced again at 12 days. Thus measurements of contraction are available for the period between 10 and 12 post-operative days in 12 intact wounds (Treatment B) and in 12 contralateral wounds from which the central granulation tissue had been excised. For the former mean contraction (estimated as skin tattoo area at 10 days minus that area at 12 days) was $2{\cdot}06 \pm 0{\cdot}16$ cm.^{2} and for the latter $1{\cdot}62 \pm 0{\cdot}28$ cm.^{2}. Unlike all the results so far reported, however, the mean of the differences in amount of contraction between sides in these animals did not reach the 5 per cent level of significance ($0{\cdot}44 \pm 0{\cdot}24$ cm.^{2}, $0{\cdot}1>P>0{\cdot}05$).

3. Changes in the Amount and Composition of Tissue within Granulation Tissue Tattoo Areas.—It has been shown above that the areas tattooed on the granulation tissue at 10 days were at that time adequately randomized, for variance within the 6 groups of wounds (three animal groups, each receiving two treatments) exceeded that between them. Tattooed granulation tissue areas were of course later altered by the treatment (A, B, or C) of the wound, and we consider now the effect of these treatments upon the amount and composition of material within the defined areas.

Results are summarized in *Table III*. In this table the probability values refer to the means of the differences between sides in a given group of

animals for the parameter concerned. These means are used as a convenient way of condensing the description of our results in the subsequent text. While reference to *Table III* is necessary to ascertain their actual level of probability, it may be taken that in the absence of any contrary indication the differences described have a less than 5 per cent probability of chance occurrence ($P<0.05$).

Twelve animals (Group I) enable areas excised from splinted wounds on the tenth day (Treatment A) day (Treatment B), while the other was biopsied with the splint undisturbed since operation (Treatment C).

Despite splinting, however, Treatment C wounds contracted considerably. At 10 days, when originally defined, their mean granulation tissue tattoo area was 1.04 ± 0.08 cm.^{2}, but by 12 days this was reduced to 0.87 ± 0.03 cm.^{2}. In Treatment B wounds, freely contracting during this period, tattoo areas diminished from 1.01 ± 0.03 to 0.62 ± 0.04 cm.^{2}. The comparison

Table III.—Weight (mg.), Composition (mg./g.), and Wet Weight per Unit Area (mg./cm.^{2}) of Granulation Tissue Tattoo Areas excised at Biopsy

(The Values for P refer to the Means of the Differences between Sides for the Tabulated Parameters)

Animal Group	Treatment	Wet Weight	Dry Weight	NCN	Collagen	Water (mg./g. wet weight)	NCN (mg./g. wet weight)	Collagen (mg./g. wet weight)	Wet Weight/Unit Area (mg./cm.^{2})
I (12 animals)	A	148·3 ± 11·1	22·4[1] ± 1·8	3·1 ± 0·3	2·9 ± 0·2	840[1] ± 3	20·6 ± 1·0	20·7 ± 1·7	150·6 ± 11·4
	B	83·8 ± 7·8 P < ·001	14·6 ± 1·3 P < ·001	2·0 ± 0·2 P < ·001	2·6 ± 0·3 P > ·6	825 ± 5 ·05 > P > ·02	24·8 ± 1·9 P > ·1	31·6 ± 3·1 ·01 > P > ·001	166·5 ± 15·1 P > ·4
II (11 animals)	B	94·3 ± 25·7	16·9 ± 1·4	2·18 ± 0·21	3·22 ± 0·49	820[1] ± 4	24·1 ± 2·2	35·1 ± 5·2	155·7 ± 14·7
	C	140·0 ± 11·8 ·01 > P > ·001	23·3 ± 1·5 ·01 > P > ·001	3·09 ± 0·35 ·02 > P > ·01	3·41 ± 0·41 P > ·7	832[1] ± 7 P > ·1	22·3 ± 2·0 P > ·6	26·2 ± 3·6 P > ·9	162·2[1] ± 15·4 P > ·9
III (10 animals)	A	136·3 ± 12·9	23·6 ± 2·5	3·12 ± 0·44	2·83 ± 0·49	827 ± 8	23·3 ± 3·3	24·4 ± 6·0	136·3 ± 12·7
	C	107·9 ± 9·7 P > ·1	20·0 ± 2·2 P > ·1	2·76 ± 0·23 P > ·2	2·84 ± 0·21 P > ·9	815 ± 10 P > ·1	26·4 ± 2·0 P > ·5	27·2 ± 2·7 P > ·6	125·5 ± 12·8 P > ·5

N.B. [1] indicates 10 animals.

to be compared with contralateral areas from wounds de-splinted on the tenth day and allowed to contract freely until the twelfth day. Mean areas within granulation tissue tattoos before incision were 0.99 ± 0.11 and 0.52 ± 0.04 cm.^{2} in Treatment A and B wounds respectively. Contraction was associated with a mean loss in wet weight of 64.5 ± 11.8 mg., in dry weight of 8.5 ± 1.3 mg., and in non-collagen nitrogen (NCN) of 1.15 ± 0.02 mg. There was, however, no appreciable loss of collagen (mean difference between sides was 0.29 ± 0.46 mg.).

Wet weight loss, unaccompanied by collagen loss led, as would be expected, to an increase in collagen concentration, which rose by 10.9 ± 3.18 mg./g. wet weight. Expressed in this way NCN concentration was unchanged. Water concentration, however, was diminished by 15.52 ± 6.31 mg./g. in contracted tissue. Finally, no difference was found between contracted and splinted material when results were expressed as mg. wet weight per unit area, i.e., the 12-day contracted tissue was no thicker than that in 10-day splinted wounds. (Since the greater part of the excised tissue was water, the assumption that specific gravity was not appreciably altered by contraction appears reasonable.)

The group of animals described above provides the most marked comparison between splinted and de-splinted wounds in our experiments. In the next group to be described (Animal Group II, of 11 animals) both sides were biopsied on the twelfth day. From one, the splint was removed on the tenth

to be made, therefore, is between more and less contracted areas rather than between contracted and uncontracted ones.

Despite this, however, freely contracted areas contained less material than those whose contraction was smaller in extent. Their wet weights were 45.7 ± 11.9 mg. less, their dry weights 6.4 ± 1.5 mg., and their NCN contents 0.91 ± 0.33 mg. less. They contained no less collagen (mean difference 0.19 ± 0.51 mg.). In terms of unit wet weight, and wet weight per unit area, no differences between sides were found.

The last group of 10 animals (Group III) enables tattooed areas from 10-day (Treatment A) and 12-day (Treatment C) splinted wounds to be compared. Again splinting was not perfect, and between 10 and 12 days mean granulation tissue tattoo area in the latter group diminished from 1.02 ± 0.04 to 0.88 ± 0.04 cm.^{2}. On Treatment A sides tattoo area was 1.00 ± 0.03 cm.^{2} before biopsy. Neither wet or dry weight nor NCN or collagen showed appreciable mean differences between sides. No differences were found for collagen, NCN, and water per unit wet weight, or for wet weight per unit area.

DISCUSSION

It is clear from our results that both the central and peripheral parts of the granulation tissue laid down were in tension. This was true for each of the three categories of wound investigated, i.e., splinted wounds at 10 and at 12 days after operation, and

wounds allowed to contract freely during the 2 days preceding biopsy on the twelfth day. Our results show unequivocally that in such wounds the central part of the granulation tissue contracted appreciably within a few minutes when freed from its surroundings by incision. The surrounding granulation tissue, bounded peripherally by the skin margins and centrally by the tattooed granulation tissue zone, simultaneously underwent a consistent diminution in area.

That the granulation tissue was thus contractile gave no proof that it was capable of developing a tractive effort sufficient to move the skin margins centripetally. But in wounds whose margins were not fixed by splints at biopsy (the 12-day freely contracted group) isolation of the central part of the granulation tissue led to an outward movement of the skin edges bordering the wound. The granulation tissue thus appeared to exert, before incision, an effort adequate to overcome the normal tension of the surrounding skin.

These results lend no support to a 'sphincter' theory, supposing that a ring of contractile material develops in or near the wound margin (e.g., Dann, Glücksmann, and Tansley, 1941). A 'sphincter' responsible for wound contraction might be expected to compress the wound content, which we have found to be in tension; neither can a 'sphincter' explain the outward movement of the wound margin following excision of granulation tissue from de-splinted wounds.

Equally, it appears that our results support the objections propounded by Abercrombie and others (1960) to the 'picture-frame' theory of contraction put forward by Watts and others (1958).

These authors proposed that in contraction the wound margins were moved centripetally by a specialized zone of cells—the 'picture-frame'. This zone, beneath the wound margin and attached to it, they believed to move over the underlying tissues and to carry the skin margin with it as it did so. The migrating cells cannot well be conceived to move over the tissues deep to the granulation tissue itself, for if they did so the latter would be in compression, and this our results show not to be the case. If, alternatively, they migrate over the deeper parts of the granulation tissue, pulling on it to move the wound margins inwards against the normal tension of the skin, then the wound content would be found, as we have shown it to be, in tension.

The 'picture-frame' theory, however, thus involving force applied peripherally to the granulation tissue to explain the tension under which the latter is found, cannot explain the decrease in granulation tissue tattoo area that we have shown to occur when contraction is hindered by continued splinting. Dots tattooed on the granulation tissue move inwards as contraction proceeds. They are not pulled outwards towards the skin margins.

We conclude that our findings are consistent with the hypothesis that granulation tissue is itself contractile (Carrel, 1910; Lindquist, 1946) and sufficiently so to mediate wound contraction (Abercrombie and others, 1956, 1960).

Two aspects of our results need further comment. First, retraction of the skin margin (following granulation tissue excision from the de-splinted wounds) failed by a large amount, as it does in the rabbit (Abercrombie and others, 1960), to re-establish the original wound dimensions. There are a number of possible explanations of this, perhaps the most likely being that a considerable amount of contractile tissue was left behind after the tattooed granulation tissue area was excised. Alternatively, the skin around the wound may have grown (Billingham and Medawar, 1955; James, 1959), or its mechanical properties have been modified.

The second aspect concerns the effect of excision of the central part of the granulation tissue on subsequent wound contraction. Whereas Abercrombie and others (1960) found in the rabbit that excision of this kind retarded later contraction, our present results reveal no such effect. The probable explanation is that we removed only about one-quarter of the granulation tissue present, whereas Abercrombie and others removed its greater part. Thus we left in situ a large amount of contractile material, and it appears that this was sufficient to accomplish contraction.

We next consider the effects of contraction on the amount and composition of material within areas demarcated on the central part of the granulation tissue by tattooing, i.e., within the granulation tissue islands excised at biopsy. The first point to be made is that the small amount of contraction occurring between 10 and 12 days in splinted wounds was associated with no detectable changes. Islands, equal in area when defined on the tenth day but excised from splinted wounds either at that time or 2 days later, contained equal amounts of material in equal concentration. No age effect was thus observed.

When, however, areas from 10-day uncontracted (splinted) wounds were compared with areas similar at 10 days, but allowed before excision to contract freely until the twelfth day, changes were observed both in the absolute amount of material present and in its composition. Thus free contraction involved loss of wet weight, dry weight, and NCN, but collagen was unaffected. Collagen and NCN increased per unit wet weight, while water diminished.

When areas, equal on the tenth day but excised on the twelfth day from splinted and contracted wounds respectively, were compared, the comparison made was between considerably contracted and less contracted material, since splinting was not completely effective. Freely contracted areas had smaller wet weights, dry weights, and NCN contents than less contracted ones, but no less collagen. Composition per unit wet weight, however, was unchanged.

It is thus clear that material is lost from granulation tissue during rapid wound contraction in the guinea-pig, and our results confirm those of Grillo, Watts, and Gross (1958) for that animal when no splinting technique is employed. Comparable material loss has been noted in de-splinted rabbit wounds by James and Newcombe (1961) and from rat wounds, at no time splinted, by Abercrombie and others (1954). Our results suggest that the total amount of collagen in the excised areas was unaffected by contraction, and that freely contracted 12-day tissue contained more collagen per unit wet weight than 10-day uncontracted tissue. This finding is in conformity with those reported for contraction over longer periods for guinea-pig wounds (Grillo, Watts, and Gross, 1958) and rat wounds (Abercrombie and

others, 1954), in neither case splinted, when collagen concentration increased with time. James and Newcombe (1961), however, reported collagen resorption in the acute contraction following desplinting in the rabbit. While the possibility remains that collagen is less labile in the guinea-pig than in the rabbit, an alternative explanation may be that the absolute amount of contraction to be accomplished is of importance. The rabbit wounds referred to above lost approximately half as much area again as did those of our guinea-pigs, and it may be that collagen resorption is seen only when contraction is adequate, in absolute terms, to evoke it.

No increase in weight per unit area was found when contracted and splinted material was compared, although James and Newcombe (1961) found for the rabbit that contraction was associated with a marked increase in this parameter. The importance of these observations lies in their significance for the theory (Cuthbertson, 1959) that contraction is due to withdrawal of material from the repair. It is clear that in both the guinea-pig and the rabbit the wound content diminishes in the plane of the skin since the skin margins approach as contraction proceeds, but not in the vertical dimension, since it becomes no thinner. A mechanism of selective withdrawal to account for such behaviour is difficult to envisage, and it appears more probable that material loss is a consequence of contraction than its cause.

In summary, our results make it likely that contraction in the guinea-pig is mediated by the granulation tissue itself, as it appears to be in the rat and the rabbit. They are incompatible with a 'sphincter' hypothesis, a 'picture-frame' hypothesis, and a 'material withdrawal' hypothesis. While our findings locate the contraction mechanism in the granulation tissue, they throw no new light on what it is. It has been shown (*see* p. 96) that contraction is not produced by collagen, and in our opinion the most likely hypothesis is that put forward by Abercrombie and others (1956), who suggested that contraction was mediated by the cells within the repair.

SUMMARY

1. Wound contraction in the guinea-pig has been studied by a splinting technique, and its effect on the amount and composition of material within demarcated areas of granulation tissue investigated.

2. When the central part of the granulation tissue in either splinted, non-contracted wounds or in those allowed to contract freely after a period of splinting, is separated from its surroundings by incision, both the central and peripheral parts of the tissue contract. In wounds without splints, the skin margins simultaneously retract.

3. Contraction is associated with loss of wet weight, water, and non-collagen nitrogen, but not of collagen.

4. The significance of these results for some proposed theories of contraction is discussed. It is concluded that the granulation tissue itself mediates contraction, and that no evidence emerged to suggest major species differences in this mechanism when results were compared with those in the literature for the rabbit and the rat.

5. The possibility exists, however, that the consequences of contraction for the wound content may be different in the guinea-pig and the rabbit, in that in the former collagen may be less labile.

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SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF FISTULA FROM THE RETAINED RECTUM TO THE BLADDER IN ULCERATIVE COLITIS

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It might be expected that a disease so destructive as ulcerative colitis would produce frequent fistulæ between the affected large bowel and neighbouring organs: yet, Cullinan and McDougall (1957) state that "Ulcerative colitis shows no tendency to fistula formation, except in the anal region. Fistula-in-ano and rectovaginal fistulæ are common." Brooke (1954) states that "fistulous communications between viscera do not occur . . . excepting rectovaginal fistulæ". However, such intervisceral fistulæ are recognized and have been recorded by Fallis and Baum (1955) in general terms as an indication for colectomy, by Rice-Oxley and Truelove (1956) in a review of complications of ulcerative colitis, by Sloan, Bargen, and Baggenstoss (1950) in a review of 2000 Mayo Clinic cases, by Ricketts and Palmer (1946) and, specifically, rectovesical fistulæ by Cattell and Sachs (1948), and Cattell (1953). No report has previously been made of such a fistula occurring after diverting the colonic stream from the rectum, and in the light of much experience that the isolated rectum may not only heal but may accept the ileal stream, it is perhaps surprising that a rectovesical fistula should occur in an isolated rectum five years after this isolation. Accordingly, this case is presented as an illustration of the capacity of the disease not only to remain much more active than would appear from clinical examination, but also to spread outside the confines of the rectum to the bladder.

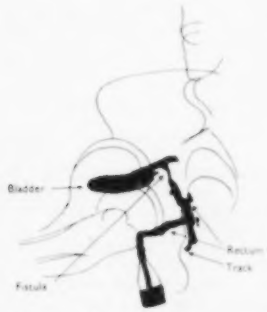

FIG. 105.—Sodium iodide injection into the rectum delineating the blind track behind the rectal stump and the irregular fistula between rectum and bladder.

CASE REPORT

Mr. L. B., at the age of 27 years, was treated for ulcerative colitis of 2 years' duration by total colectomy (Mr. Dickson Wright) in December, 1953: at this operation a rectal stump of 6 cm. was left with a view to restoration of continuity at a later date. Regular examinations were carried out until May, 1956, by which time only slight superficial disease remained in the rectum and he was expected soon to be ready for ileorectal anastomosis. At the end of February, 1957, he had a hæmorrhage from an ulcerated area at the apex of the rectal stump about 3 cm. of which had to be resected. The remaining stump showed no sign of active disease thereafter, and by the end of 1957 restoration of continuity was again considered.

In February, 1958, he had an episode of urinary frequency and dysuria for 48 hours, followed by 48 hours' hæmaturia: he was given 'Gantrisin' by his private doctor and was relieved of all his symptoms. Four weeks later the symptoms returned and culture of the urine produced *B. coli* only. Both these episodes were accompanied by pus and blood from the rectum, disappearing *pari passu* with the urinary symptoms. On the second occasion the urine was rendered sterile with chloramphenicol and cystoscopy was performed: this showed only the appearances of generalized cystitis: rectal examination at this time showed some stenosis at the anus but no active disease: during the cystoscopy none of the irrigating fluid appeared at the rectum. He was discharged symptom-free, only to come again in June, 1958, with a profuse watery rectal discharge: this discharge ceased from time to time to be followed by a recurrence of his urinary symptoms: urine

cultures produced *B. paracoli* and proctoscopy showed what appeared to be urine at the apex of the rectal stump. Distending the rectal remnant with sodium iodide demonstrated radiologically a blind track behind the rectum and an irregular fistula from the apex of the rectum to the bladder (*Fig.* 105).

On June 23, under spinal anæsthesia, the rectal stump was dissected out from below, closing the vesical connexion with catgut sutures (Mr. Dickson Wright).

Following this procedure his recovery was in every way uneventful, and he has had no further trouble. Histologically the rectum showed complete loss of mucosa with replacement by granulation tissue.

COMMENT

This case is presented to illustrate the most unusual complication of the disease, a rectovesical fistula, and the evident progression of the disease despite relief from insult by colonic content and clinical appearance suggesting resolution.

Acknowledgements.—I am much indebted to Mr. Dickson Wright, under whom this case was admitted, for permission to publish the details, and for help in the preparation of the paper.

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ADDISONIAN PIGMENTATION DUE TO EXTREME PYLORIC STENOSIS BY A MUCOSAL DIAPHRAGM

BY HENRY B. YOUNG, WOLVERHAMPTON

PYLORIC stenosis in an adult, due to a mucosal diaphragm, is exceedingly rare. At the time of operating on the case described below, in 1957, only 3 others appear to have been published (Sames, 1949; Rota, 1953; Passalacqua and Romero, 1955). Since then Rhind (1959) has described 7 more cases and Digby Chamberlain and Addison (1959) 2 others. The total number of cases of this condition, therefore, is extremely small and many of its features have not been clearly pictured.

The following case is worth reporting, not only on account of its rarity, but because of the presence of manifestations not yet noted and the extremity of the clinical state, due to the patient's determination to avoid medical treatment while she had any strength to do so.

CASE REPORT

Mrs. Sarah Jane G., aged 53 years, was admitted on June 19, 1957, to the medical ward, under the care of Dr. E. J. Blair, with the following history. She had been fit and well all her life and could eat anything, but for several years her appetite had become smaller and she had had to eat a very moderate quantity, although of any type of food. She had never had any pain. She had always been slight. She had had all her teeth out in 1948 and mastication had been less satisfactory since then, matching her appetite. Menopause was at 43 years of age. Two months prior to admission she had caught a cold and following this had developed complete anorexia, nausea, and vomiting of everything she ate. After two weeks of this, she improved sufficiently to keep fluids down, but still lost weight, became very weak, and fainted on three occasions. In the last three days vomiting had recurred and persisted, day and night, and was accompanied by heartburn, relieved by alkalis and sitting up, but not by food. She had a slight, non-productive cough.

ON EXAMINATION.—She was thin and had lost much weight and now weighed only 5 st. 4 lb. Her skin was generally pale and there were, in marked contrast to this, areas of dark pigmentation on the face, neck, forearms, bathing-drawers area, and upper calves (*Fig.* 106). The oral mucosa, especially on the inside of the cheeks, also showed this marked pigmentation (*Fig.* 107). Large waves of peristalsis were visible at times, passing from left to

FIG. 106.—Showing areas of cutaneous pigmentation.

right across the whole abdomen. No other abnormality was found. Blood-pressure 120/70 mm.

Clinical Impression.—The classical features of pigmentation (including mucous membranes), weakness, wasting, anorexia, and moderate hypotension were suggestive of Addison's disease. The large stomach and visible peristalsis were thought to be due to superimposed pyloric stenosis, possibly more obvious owing to her thinness and alimentary upset from the Addison's disease.

FIG. 107.—Showing buccal pigmentation on inside of cheek.

INVESTIGATIONS.—Serum-electrolytes: Sodium, 320 mg. per 100 ml.; Chlorides, 410 mg. per 100 ml.; Potassium, 23·5 mg. per 100 ml.; Carbon-dioxide-combining power, 95·9 ml. per 100 ml.

Hb, 85 per cent; W.B.C. 7400 per c.mm. (Polymorphs 74 per cent, Lymphocytes 22 per cent, Monocytes 4 per cent).

Urine: Sodium, 3·4 g.; Chlorides, 0·17 g.

Straight radiographs of the chest showed no sign of tuberculosis, and those of the abdomen no suprarenal calcification.

PROGRESS.—Three days later she vomited green fluid and her blood-pressure fell to 80/60 mm. She was given two pints of intravenous saline and improved greatly and her blood-pressure rose to 105/60 mm. She was put on tablets of cortisone acetate, 25 mg. daily. She felt so well, two days thereafter, that she took her own discharge. Despite her promises to attend the Out-Patient Department and requests from the hospital for her to do so, she did not appear for check up, merely writing to say that she was well and gaining weight.

She remained well for four months, when she 'caught a cold' and began vomiting again. This was mild at first, but after ten days became severe and intractable and she began to feel unwell. After three days of this vomiting she became comatose, and when this had persisted for twenty-four hours she was re-admitted to hospital on Nov. 9.

ON EXAMINATION.—She presented the same picture as before, but in addition she was comatose, but just rousable. She was very wasted and grossly dehydrated. Her blood-pressure was 70/30 mm. of mercury.

She was thought to be in an Addisonian crisis, possibly due to a secondary in the adrenals, from a gastro-intestinal neoplasm.

She was given hydrocortisone, 20 mg. intramuscularly, and intravenous saline.

FIG. 108.—Showing pressure required to extrude water through pin-hole meatus.

Her electrolytes the next day were: Sodium, 220 mg. per 100 ml.; Chlorides, 450 mg. per 100 ml.; Potassium, 11 mg. per 100 ml.; Carbon-dioxide-combining power, 82 ml. per 100 ml. Blood-urea, 115 mg. per 100 ml. Glucose (at 11 a.m.), 118 mg. per 100 ml.

Six days later there was little aspiration, but her blood-pressure remained 90/60 mm. She then vomited black material and her hæmoglobin was found to be 40 per cent. Electrocardiograph was normal. She reacted to three pints of blood with an itchy, erythematous rash on her back, so rectal saline was commenced, her blood-pressure being 80/50 mm.

In view of the failure of medical measures, a surgical opinion was sought, and exploration was offered if the hæmoglobin and blood-pressure could be raised further.

On Nov. 26 her blood-pressure was 105/68 mm., her hæmoglobin 65 per cent, and exploration was carried out (H.B.Y.) under general anæsthesia (Dr. J. R. Elliott).

AT OPERATION.—A vast stomach was found filling the whole abdomen. This was clearly due to stenosis, as some weak peristalsis was present. There was, however, no visible or palpable abnormality at the pylorus. A rapid partial gastrectomy (right to left, antecolic, after excision of the lesser curve) was carried out.

Examination of the excised specimen showed a most extreme stenosis due to a mucosal diaphragm. On filling the stomach with water at the upper end much pressure was required to extrude a few drops of the fluid through

the pin-hole meatus, as can be seen in the illustration (*Fig.* 108) by the depth of the pressure marks of the fingers. The minute, secondary membrane partly across the pin-hole was dilated by the probe (*Fig.* 109). The mucosa in the pyloric region was, as also seen in *Fig.* 109, flattened and pebbled in appearance, in contrast to the rugose mucosa proximally.

PATHOLOGICAL REPORT (Dr. A. G. Marshall).—"The specimen is an unfixed stomach. It is greatly enlarged and this portion measures approximately 15 cm. along the lesser curve and 34 cm. along the greater curve. Its wall is thickened and its external surface appears normal. When the specimen is opened only a pin-hole hiatus can be seen in the pyloric end of the mucosa, although the pylorus

FIG. 109.—Showing secondary membrane across pin-hole dilated by probe, and flattened, pebbled appearance of mucosa in pyloric region.

appears macroscopically to be quite wide. This pin-hole can of course be seen in the duodenal mucosa which abuts on the gastric mucosa at this point and in each case they seem to end in a round stocking like manner.

"There is a flattened irregular ulcer measuring 4 cm. in diameter on the anterior wall about 8 cm. from the pylorus and a smaller one nearby. There is a good deal of induration of the wall at this point. I found no enlarged lymph nodes on either curvature.

"Sections of the ulcer show no evidence of malignancy. There is a tremendous œdema of the submucosa and the muscle is hypertrophied."

POST-OPERATIVE PROGRESS.—She made a steady convalescence from this, though her blood-pressure was slow to return to normal, being 100/60 mm. of mercury on discharge twenty-four days later. Her blood-urea and serum electrolytes had become normal by this time.

Thorn's Test (eighteen days after operation), Eosinophil count—320 per c.c. ACTH 0·5 mg. subcutaneously, Eosinophil count—430 per c.c.

Water Excretion Test—Robinson, Power, and Kepler, 1941 (16 days after operation), Factor: 16·7.

PRESENT STATE, two years after operation: The patient looks fit and well covered and has an excellent colour. She has gained 2 st. in weight and is eating a normal diet. She says she feels like a new woman.

DISCUSSION

This case presents one feature not yet described in this condition (1) and underlines the relation of two others in relation to it (2, 3):—

1. That mucosal stenosis can lead to such a slow, but extreme state of malnutrition that pigmentation of a type almost pathognomonic of, and chemical changes suggestive of, Addison's disease appear, presumably due to deficiencies similar to that of pellagra.

2. That where the opening is small, but compensated, upper respiratory tract infection can precipitate symptoms and, indeed, cause almost fatal blockage, owing to inflammatory œdema and obstruction by swollen mucosa.

3. That loss of natural teeth and a temporary state of edentulousness, with subsequent inadequacy of mastication, can initiate slow decompensation owing to mechanical difficulty and, perhaps, traumatic œdema from unmasticated food, which ultimately leads to clinical symptoms.

Looking at the specimen the diaphragm was so even and normal to inspection and palpation that it was difficult to see how scarring from annular ulceration at the pylorus could have been the cause, as suggested by Rhind (1959). Further, with such a process of ulceration and healing in the active narrow canal, and the patient on a normal, if not generous, diet, it seems unlikely that she would have had no previous symptoms, yet she was quite clear that she had had none.

The even, flattened, pebbled appearance of the pyloric mucosa was striking and this appearance was noted by Rota (1953) in his case, in which numerous sections of the antrum, with these changes, showed well-marked chronic gastritis with well-marked injection of the lamina propria, with lymphocytes, reduction in size, number, and depth of the glands, and thickening of the muscularis mucosæ. He found complete absence of scarring in this area.

The presence of a simple gastric ulcer some distance from the pylorus seemed a concomitant product of the stenotic state and general asthenia, rather than the cause of it.

The pigmentation and biochemical changes must have been primarily due to deficiency in origin, as they resolved completely after operation. It may, however, also be that in such extreme deficiency a degree of adrenal hypofunction is also present temporarily.

SUMMARY

A case of extreme pyloric stenosis due to a mucosal diaphragm is noted in which one of the most striking presenting features was marked, widespread Addisonian type of pigmentation of the skin and oral mucosa—a feature not previously described.

Decompensation of the balance between the obstruction of the minute stoma and the forces of gastric peristalsis was initiated by loss of her own teeth and completed, on several occasions, by upper

respiratory catarrh and had led to an almost final catastrophe—coma.

Partial gastrectomy relieved this extreme syndrome.

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NEURILEMMOMA OF THE DUODENUM

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WHILE neurilemmomas are encountered not uncommonly in various parts of the body, notably in connexion with the acoustic nerve and the main nerves of the flexor aspects of the body, they are much less common in the alimentary canal and quite rare in the intestines. Stout (1935), in a paper on 50 personal cases of peripheral neurilemmomas, was only able to find 3 in the whole of the alimentary tract and these were all situated in the stomach. In a larger series of all that had been reported in world literature, a total of 246, only 2 were present in the first part of the duodenum—the cases of Delagénière (1926) and Lemonnier and Peycelon (1933). It is, therefore, fitting to add one more to this scanty series of rare tumours.

CASE REPORT

I was first called to see this patient during the early part of October, 1959. She was a frail old lady of 76 years and had been complaining of an abdominal swelling for the past 14 months. This was accompanied by a certain amount of epigastric pain which was eased when she lay down, and for this reason she had taken to her bed. The pain was of a constant throbbing nature and referred to the anterior abdominal wall. She had some difficulty with respiration. In spite of some loss in weight there had been no loss of appetite. There had been no suggestion of obstructive symptoms and no history of jaundice.

Examination at that time showed a well-defined mass about the size of a Jaffa orange to the right of the umbilicus. It was firm, oval in shape, slightly movable, and not tender. Rectal examination was negative. She had a normal temperature. There were no signs of lumps anywhere else. Her blood-pressure was 150/80 mm. and she looked anæmic.

I made a provisional diagnosis of a renal tumour.

Her urine contained albumin and a few pus cells and the blood-picture on admission to hospital was recorded as: Hæmoglobin 5·0 g. per cent, P.C.V. 16 per cent, W.B.C. 15,000 per c.mm., Polymorphs 78 per cent, Lymphocytes 20 per cent, Monocytes 2 per cent, Reticulocytes 20 per cent, Blood-urea 47 mg. per cent.

Red cells show fairly well-marked anisocytosis and moderate hypochromia with increased polychromesia. Appearances are consistent with iron deficiency and most suggestive of recent blood-loss.

She also had a positive occult blood.

The first investigation was an intravenous pyelogram and the report came back as follows: "Both kidneys excrete the opaque medium without delay and appear normal. There is a strange 'kink' in the right ureter, but it is not causing obstruction and I do not think it is of clinical significance. Opacities in the right side of the pelvis are probably glandular and there is no radiological evidence of an abdominal mass."

This was followed by a barium enema and this report came back: "Large bowel N.A.D. The hepatic flexure is depressed by a palpable mass."

I was still puzzled as to the nature of the condition and thought that a retrograde pyelogram and screening would help.

FIG. 110.—Patient three months after operation.

On cystoscopy the bladder was quite normal with normal ureteric orifices and effluxes. A catheter was readily passed up the right ureter and she was transferred to the X-ray Department, where dye was injected while screening and the mass palpated. It was definitely

confirmed that the tumour was extrarenal and by combining with the examination a barium enema, its relation to the colon and kidney could be more accurately defined. By this time it was obvious that it was unlikely that any further investigations could help in the diagnosis. She was prepared for a laparotomy which was carried out on Aug. 20, 1959.

Six pints of blood had raised her hæmoglobin up to 12·7 g. per cent and, under a very skilful anæsthetic administered by Dr. Waterfall, the abdomen was opened through a right paramedian incision. At first sight the

FIG. 111.—Neurilemmoma of second part of duodenum.

mass had the appearance of a retroperitoneal growth lying posterior to the second part of the duodenum with the latter stretched over it. There was no evidence of any metastases.

The peritoneum to the lateral side of the duodenum was incised and the duodenum rotated medially. It was then realized that the growth was embedded in the head of the pancreas. Its nature still remained obscure. An attempt to dissect it out caused severe hæmorrhage. It seemed to be intimately attached to the head of the pancreas and to the second part of the duodenum. I was then of the opinion that it was most likely to be a carcinoma of the head of the pancreas and the only solution was to do a Whipple operation. The tumour with the duodenum and head of pancreas and lower end of the bile-duct was resected. The proximal end of the jejunum was brought through the gap and the common bile-duct was anastomosed to its extremity, the neck of the pancreas implanted into its side and lower down the anastomosis of the stomach was completed. A drainage-tube was placed down to these anastomoses and brought out by an independent opening to the right of the paramedian incision and the abdomen closed.

The patient stood the operation very well. There was some leakage of bile a few days later, but this soon cleared up and she left hospital about a month after the operation.

I saw her again three weeks ago and she said that it was a long time since she felt so fit and free from all discomfort. She was profuse in her thanks and felt she had been granted a new lease of life (*Fig.* 110).

The report from Dr. Ellis, the Pathologist, was as follows (Sept. 2, 1959): "Duodenum measuring 17 cm. along with attached mass presumably head of pancreas measuring 8 × 8 × 6 cm. In the centre of the portion of this duodenum there is an opening 3 cm. long in the long axis and 1 cm. wide. This leads to what appears to have been a cavity within the tumour, probably a dilated duct. The tumour mass on gross section was found to consist of fairly firm white tissue with softened areas containing hæmorrhage (*Fig.* 111).

"Histological examination shows a well-encapsulated benign tumour consisting of large spindle cells with extensive areas of degeneration. The tumour does not appear to be in the pancreas but pancreatic tissue is present

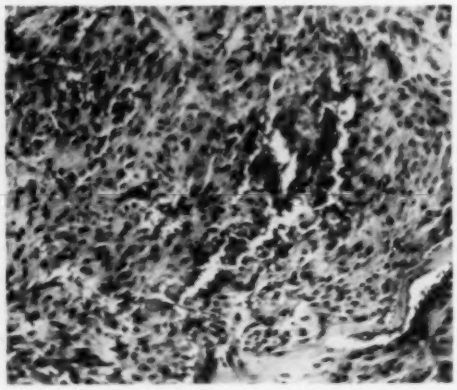

FIG. 112.—Microsection of neurilemmoma. (× 67·5.)

in and close to the capsule. This is probably a neurilemmoma of the duodenal wall." (*Fig.* 112.)

Probably the best account of the peripheral neurilemmomas is that given by Stout (1935). He found stigmata of Von Recklinghausen's disease in 18 per cent of his cases. He found that these tumours were always encapsulated except in the case of some of the visceral lesions, which appear to have limited powers of infiltrative growth. He stated that when seen fresh at the time of removal they have a pink, yellow, or pearl grey aspect. The cut surfaces bulge sometimes, but not very frequently. Degenerative cysts are sometimes present and hæmorrhages are frequent.

In his studies Stout states that the symptoms are not conspicuous apart from the presence of the mass. Some complain of pain but the diagnosis has rarely been made possible without histological examination.

It is doubtful whether they ever develop sarcomatous changes as has been maintained by some and when successfully removed usually result in a permanent cure.

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A RENO-JEJUNAL FISTULA

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THE occurrence of a fistulous connexion between the kidney or ureter and an adjacent organ or the body surface is a serious condition, and presents a formidable surgical problem. The condition was first described by Hippocrates in the fifth century B.C., and Abeshouse (1949) was able to collect a total of 340 cases of renal fistula from the world's literature.

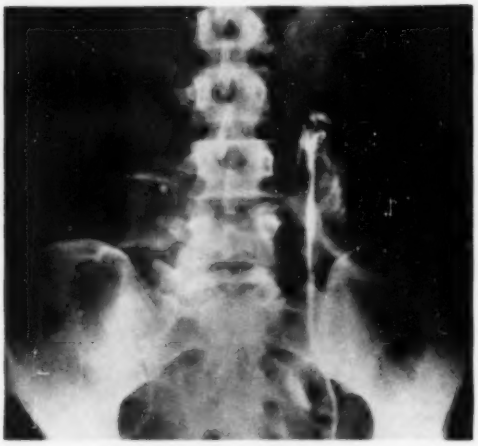

FIG. 113.—Retrograde pyelogram showing fistulous connexion between left kidney and upper jejunum.

Since then, isolated cases have been reported by King (1950), Jones, Melendy, and Flynn (1953), Briggs and Neale (1953), Bloom (1954), and North, Livingston, and Lovell (1956).

In the case here presented there was a fistula between the left kidney and a loop of the upper jejunum. The writer has been unable to find any previous case report of reno-jejunal fistula in the literature.

The rarity of this condition and the perplexing diagnostic and surgical problems encountered warrant the presentation of a single case and a brief consideration of its clinical features and treatment.

CASE REPORT

Mrs. E. D., aged 30 years, was admitted to Walton Hospital, Liverpool, with a history of pain in the left loin radiating to the groin for four days. She had had rigors. She had a similar, though less severe, attack six weeks previously, but had no micturition disturbance.

ON EXAMINATION.—The temperature was 103·8° F. and the pulse-rate 120/min. Her general condition was fair. There was tenderness with guarding in the left loin and left side of the abdomen, but no mass could be felt.

Investigations.—Hæmoglobin, 72 per cent (M.R.C.), W.B.C., 16,000 c./mm., 87 per cent neutrophils. M.S.S.U., scanty leucocytes and R.B.C.s only. Straight radiograph (renal tract): "left kidney shadow not well visualized. No opaque renal calculus seen."

Excretion pyelography (Dr. John Winter): "The right kidney functions well and shows a normal pyelogram. No function is detected on the left side."

A course of chloramphenicol, 250 mg. six-hourly, was instituted, her general condition improved, and the pyrexia tended to subside.

A cystoscopy and left retrograde pyelogram was performed one week later. This was reported (Dr. John Winter) (*Fig.* 113): "The left ureter is catheterized as far as the transverse process of L.3. Dye is present in the ureter distal to this point. There is dye in the

FIG. 114.—Barium follow-through demonstrating fistulous track between upper jejunum and left renal pelvis.

FIG. 115.—Kidney, showing dark inflamed pelvis, and lighter fatty tissue, replacing kidney parenchyma. Central marker in ureter opening, left marker showing fistulous opening.

adjacent loop of small bowel, indicating a fistulous communication."

The following day further examination revealed a perinephric abscess pointing in the left loin. This was incised and drained of much foul-smelling pus. Culture of this showed a growth of *Staph. pyogenes* and paracolon bacillus.

The patient's general condition improved and the pyrexia subsided.

A barium meal (*Fig.* 114) performed three weeks later was reported: "Stomach and duodenum show normal appearances. A fistulous track is demonstrated between the upper jejunum and the left renal pelvis."

The abscess had almost ceased to drain and the patient was discharged from hospital to out-patient care, where a further excretion pyelogram two months later again showed no function of the left kidney.

The patient was re-admitted eight months after the first onset of symptoms for exploration of the left kidney.

AT OPERATION.—Left renal incision, excising old scar. Many adhesions were found around the kidney, which was freed. There was fistulous communication between a loop of the upper jejunum and the anterior aspect of the kidney. The fistulous track was divided, the opening in the bowel repaired, and nephrectomy performed. The jejunum was otherwise normal and was replaced in the abdomen, and the peritoneal defect closed.

The patient's post-operative progress was satisfactory and she has since given birth to her third child.

PATHOLOGICAL REPORT (Dr. W. H. Wodzinski) (*Fig.* 115).—"Kidney largely replaced by firm fatty tissue continuous with the perinephric fat. The calices and renal pelvis are dilated and there is a fistula between the pelvis and small bowel. Sections did not reveal any recognizable renal tissue. Sections from the region of the fistula show a large amount of fibrous and granulation tissue. No neoplasm seen."

DISCUSSION

Aetiology.—A simple anatomical classification of these fistulæ based on the point of origin and exit is recommended by Abeshouse (1949). In the great majority of cases the origin is in the kidney or ureter, although in very rare instances there is a reversal of the point of origin, which arises in a neighbouring organ and terminates in the kidney or ureter.

The spontaneous group of reno-visceral fistulæ result from an inflammatory process in the kidney which invades an adjacent viscus. A perirenal abscess may develop first, and this may later rupture into the viscus.

Other fistulæ result from surgical intervention or trauma.

In the present case presumably an acute left pyonephrosis resulted in a large perinephric abscess which on its anterior aspect caused inflammatory adhesions to a loop of jejunum, and later this abscess burst into the bowel causing the fistula. Still later a perinephric abscess formed posteriorly and was drained in the loin.

Diagnosis.—A careful history is helpful in diagnosis, particularly in respect of the presence of renal stone.

There are no characteristic symptoms. However, there may be severe shock or toxæmia associated with extravasation of urine and later the formation of a perinephric abscess. Micturition disorders are unusual, although some cases have been described in which severe frequency and dysuria were pronounced.

Special Investigations.—

Retrograde pyelography is the most valuable investigation and often shows the fistula and also the state of the kidney.

Excretion pyelography is a harmless and efficient form of investigation of renal injuries with or without a fistula, but depends on the ability of the affected kidney to excrete the dye which may be shown beyond the kidney confines. Abeshouse (1949) did not find a single case where this investigation revealed a spontaneous type of renal fistula.

The use of barium enemata and meals, and injection of iodized oils along a renal fistula pointing on the surface of the body, may all be diagnostic.

In the present case the diagnosis was made by retrograde pyelography and confirmed by barium meal and follow-through.

Treatment.—Prophylactic treatment consists of early treatment of renal infections and calculi and prompt drainage of perinephric abscesses. Also adequate drainage following certain conservative operations on the kidney such as pyelo(nephro)-lithotomy, or partial nephrectomy, is important.

Operation offers the only real hope of relief or cure of the established condition.

In most cases preliminary drainage of a perinephric abscess is essential, and this decreases markedly the difficulties and risks of this subsequent exploration of the kidney.

The usual procedure combines exploration of the kidney, definition and excision of the fistula, and repair of the organ concerned.

In most cases it is necessary to remove the kidney because of advanced destruction, although in a few cases of reno(ureteric)-cutaneous fistula due to impacted calculus, the kidney may be conserved.

The present case shows the value of the staged procedure in treatment of these cases.

SUMMARY

A case of reno-jejunal fistula between the left kidney and the upper jejunum is presented. The fistula resulted from an acute pyonephrosis causing an anterior perinephric abscess which ruptured into the loop of jejunum. The fistula was demonstrated by retrograde pyelography and barium meal and follow-through. Preliminary drainage of a perinephric abscess and later exploration of the kidney with excision of the fistula and repair of jejunum and nephrectomy was performed. The post-operative progress was satisfactory. The present writer has been unable to find a report in the literature of any reno-jejunal fistula.

The clinical features, diagnosis, and treatment are reviewed.

I wish to thank Mr. R. A. C. Owen, consultant surgeon, Walton Hospital, Liverpool, under whose care the case was admitted, for his kind help in the preparation of this paper.

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SURGICAL RESEARCH SOCIETY

THE fourteenth meeting of the Society was held at the Royal Victoria Infirmary, Newcastle upon Tyne, on May 5 and 6, 1961, under the chairmanship of Mr. Selwyn Taylor. (The President, Mr. Hedley Atkins, was in Australia as Sims Travelling Professor.) The following papers were presented and discussed:—

1. D. N. WALDER, Newcastle: "Severe Air Embolism following Short Exposures to Pressure".

Radiographic investigations had suggested that severe air embolism could follow even correct decompression from compressed air. The possibility that this might be due to the passage of air trapped within the lung into the pulmonary veins was investigated in animals. Decompression after short exposure to even 2 atmospheres absolute pressure may, under some circumstances, be a danger. This matter should be borne in mind by those contemplating operating and treating patients in compressed air.

2. F. E. WEALE* (Sir R. C. Brock), Guy's Hospital: "Pressurized Oxygen in Total Body Perfusion".

The improvement in oxygenation of blood derived from pressurization of the oxygenator and pre-cooling of the blood had been investigated in 40 dogs. An oxygenation chamber had been designed in which the gas pressure could be raised to 3 atmospheres absolute. The technical problems of decompression of blood from such pressures to suitable arterial perfusion levels had been studied, and the advantages of pressurized oxygen were demonstrated experimentally. Despite theoretical reasons for believing that pre-cooling of blood prior to oxygenation might be advantageous, because of the shift in the oxygen dissociation curve, it was not found to be so in practice.

3. A. R. GHANI* and D. J. TIBBS, Newcastle: "Regeneration of Vascular Endothelium".

In plastic arterial prostheses there is, from an early stage, a selective laying down of cells from the blood-stream in the mural thrombi lining the plastic material; by the use of diffusion chamber techniques it has been found that mononuclear white blood-cells are capable of transformation into endothelial-like cells. Studies had been made upon woven plastic arterial substitutes lined by, or ensheathed in, millipore filter membrane and nylon film to prevent cellular infiltration from without; these plastic 'grafts' were too long to allow ingrowth from the ends to affect the centre portion during the period of the experiment. The cell formations deposited purely from the blood-stream indicated that mononuclear cells were capable of lining fibrinous lacunæ and forming vascular spaces and primitive capillaries. The fibrous tissue support of new intima originated by ingrowth from neighbouring tissues and not from free-circulating cells.

4. W. COOK,* R. CURRAN,* and J. B. KINMONTH, St. Thomas's Hospital: "Comparison of Materials for Repair of Cardiac Defects".

Defects made in the right ventricular outflow tract in the dog had been repaired with terylene cloth, formalinized canine vein (homograft), or formalinized human pericardium (heterograft). The results had been studied at periods up to one year. Contraction always occurred unless part of the pulmonary artery and valve ring had been excised as well as muscle from the right ventricle. Pericardium was supple, blood-tight, and best to work with, but the end-results favoured terylene. This united with least foreign-body reaction and the best internal lining and support from host tissues.

5. E. J. GUINEY,* J. P. MCMULLIN,* and J. A. MEGIGAN* (P. A. M. F. Fitzgerald), Dublin: "Blood-loss to the Experimental Animal during Profound Hypothermia with Extra-corporeal Circulation".

Profound hypothermia had been induced by the Drew technique in 35 acute experiments in pigs. Circulation had been arrested when nasopharyngeal temperature reached 15° C. The blood-loss, which at times equalled the total blood-volume of the animal, occurred during the cooling phase. There was partial recovery during re-warming. Studies of the portal venous bed and portal venous pressure after portocaval anastomosis revealed that the 'lost' blood was located in the portal venous system. The suggestion that the cause was an anaphylactoid reaction due to antigen in donor blood was supported by the response to antihistamine (chlorpheniramine maleate), which reduced both portal pressure and blood-loss. The site of the venous obstruction might be intrahepatic or at the portal or hepatic veins.

6. F. W. GAIRNS,* H. S. GARVEN,* and G. SMITH, Glasgow: "Alterations in Peripheral Nerves of the Lower Limb in Chronic Occlusive Vascular Disease".

In an attempt to find the cause of the paræsthesiæ and more rarely the intractable pain of 'ischæmic neuritis' a histological study had been made of the nerve-fibre changes accompanying occlusive vascular disease of the lower limbs. The peripheral nerves in ischæmic neuropathy showed increasingly less myelinated fibres as the acral parts were reached. There was also alteration in the spectrum of the fibre sizes so that smaller fibres assumed dominance while there was diminution or less of the larger, more rapidly conducting myelinated ones. Fibres of the amyelinate series were nevertheless still abundantly present. This state of fibre dissociation was associated with other spontaneously painful states such as post-herpetic neuritis. Anoxia may cause the 'firing off' of impulses in the surviving fibres giving rise to pain. Alternatively, with the loss of insulation of the fibres following the demyelination process, the possibility of fibre 'cross-talk' arises, and this, by stimulating impulses in pain afferents, could give rise to spontaneous pain.

7. W. R. CATTELL,* A. G. SPENCER,* G. W. TAYLOR, and R. W. E. WATTS,* St. Bartholomew's Hospital: "The Physiology of Renal Oxalate Excretion".

The method by which the kidney excretes oxalate had been investigated in lightly anæsthetized dogs. The renal clearance of C-14 oxalate had been measured simultaneously with the glomerular filtration rate and the effective renal plasma flow, and the effects of osmotic diuresis, of urinary *p*H changes, and of selective inhibitors of tubular transport on the C-14 oxalate clearance had been studied. Further data had also been obtained by stop-flow analysis. It was concluded that the oxalate ion was excreted by a combination of glomerular filtration and proximal tubular secretion, and that tubular reabsorption also occurred.

* Those members whose names are marked with a star were introduced to the Society at the meeting.

8. H. B. TORRANCE, R. P. DAVIES,* and P. B. CLARK,* Manchester: "A New Method of detecting Unilateral Renal Ischæmia in Hypertension".

Radio-active potassium and rubidium share the unusual property of exchanging with intracellular potassium during a single circulatory transit. After intravenous injection the specific activity of any tissue depends on the perfusion rate, i.e., on the fractional distribution of the cardiac output. The kidneys receive approximately 20 per cent of the injected dose and, because of the high ratio of blood-flow to renal mass and the relative proximity to the surface, external scintillation counting can be employed to detect unequal distribution of renal blood-flow. The mean differences were as follows: Controls (21 cases)—2 per cent (S.D. 9 per cent); unilateral nephrectomy (17 cases), Left—42 per cent (S.D. 14 per cent), Right—29 per cent (S.D. 14 per cent). Hypertensives (43 cases): renal artery stenosis (4 cases)—34 per cent (S.D. 5 per cent); miscellaneous unilateral renal lesions (8 cases)—31 per cent (S.D. 8 per cent); others (31 cases)—within normal range. This technique provides a simple and reliable method of detecting abnormalities of renal blood-flow in hypertension.

9. J. E. S. SCOTT* (A. G. R. Lowdon), Newcastle: "The Structural and Dynamic Effects on the Upper Urinary Tract of the Dog of Prolonged Vesico-ureteric Reflux".

Vesico-ureteric reflux had been produced by resection of the intravesical mucosal flap valve leaf. Monthly cystography had been performed to determine the state of the upper urinary tract, and the blood-urea had been measured and urine cultured at the same times. Cinécystography had been undertaken on each surviving dog. Four dogs remained alive and healthy after 10, 8, 5, and 3 months. Reflux could be demonstrated cystographically in all, but there was no dilatation of the upper urinary tracts. The blood-urea levels remained normal and the urine sterile. Reflux, therefore, had not affected the upper urinary tracts in these dogs. Cinécystography suggested that reflux appeared at an early stage of bladder filling in ureters with diminished peristaltic activity.

10. J. SWINNEY,* B. J. TOMLINSON,* and D. N. WALDER, Newcastle: "Urinary Tract Substitution".

11. A. O. ADESOLA,* J. T. WARD,* M. G. McGeown,* and R. B. WELBOURN, Belfast: "Hyperparathyroidism and the Alimentary Tract".

In 70 patients who had undergone parathyroidectomy for primary hyperparathyroidism 30 (43 per cent) had had gastro-intestinal symptoms. In 15 (21 per cent) they had been of ulcer type and in 8 (11 per cent) of these there had been proved duodenal ulcers (males 7/31—23 per cent). Operation had relieved symptoms in all but one. Other symptoms, which had usually been relieved by operation, included anorexia, nausea, vomiting, and constipation. Basal and augmented histamine secretions of gastric acid had been measured before and after operation in 5 cases. Basal secretion was reduced in every case (mean fall = 30 per cent; $P < 0.05$), but the augmented histamine secretion was unaffected ($P < 0.4$). In 5 dogs with denervated gastric pouches parathormone (200–300 I.U. per day subcutaneously) was very toxic but raised the serum calcium and, in 3, appeared to cause simultaneous transient stimulation of acid secretion in the basal juice.

12. W. BURNETT and CATHLEEN GORDON,* Glasgow: "The Pathogenesis of Gall-stones".

Human bile had been analysed to assess the importance of various factors thought to be concerned in the formation of gall-stones. Particular interest had been taken in cholesterol and associated sterols, both free and esterified, phospholipid, and the bile-salts which had been estimated by partition chromatography as glycine or taurine conjugates of cholic, chenodesoxycholic, or desoxycholic acids (Sjovall, J. (1959), *Clin. chim. Acta*, **4**, 652). The original bile-salt technique had been modified slightly and found reliable. A normal range had been established for these constituents of bile in man. Analysis of bile obtained at operation from patients with cholelithiasis showed that abnormally low values for phospholipid and total bile-salts were present in the majority of cases, and that the output of cholesterol was significantly increased in 50 per cent. The implications of these findings were discussed with regard to the importance of the lecithin–bile-salt complex and the metabolic and physico-chemical relationship between cholic acid and cholesterol.

13. R. S. SNELL* (A. G. R. Lowdon), Newcastle: "The Influence of Trauma on the Activity of Melanocytes in the Skin".

Trauma and irritation can increase melanin pigmentation and it has been suggested that trauma probably plays a part in stimulating the change-over of a benign melanoma to one with malignant tendencies. Controlled histochemical experiments had been undertaken for accurate assessment of the effects of physical trauma, acid, and alkali, and of ultraviolet, infra-red and X-ray irradiation on the melanocyte counts, the morphology of the melanocyte and the amount of free melanin present in the skin. Eighty-four guinea-pigs had been used and both skin sheets and vertical skin sections had been studied. The melanocytes had been demonstrated by means of the Dopa reaction. All these external irritants were found to stimulate melanogenesis.

14. C. Q. HENRIQUES* (J. G. Murray), King's College Hospital: "The Vertebral Veins and the Spread of Cancer".

Malignant tumours of the breast, thyroid, kidney, and prostate metastasize readily to the axial skeleton. This may partly be due to the filtration of a proportion of the systemic venous blood through the vertebral column. The present study, using resin cast techniques, demonstrated extensive communication between the caval and azygos systems and the internal vertebral venous plexus. Experiments on dogs demonstrated that there was a reflux of blood from the caval and azygos veins into the vertebral system when intrapulmonary pressure was increased. Measurement of caval pressure changes in man occasioned by straining or coughing indicated that a similar reversal of flow into the vertebral veins was likely to occur.

15. J. L. HAYWARD and R. D. BULBROOK,* Guy's Hospital: "Abnormalities in Steroid Hormone Excretion in Early Breast Cancer".

A discriminant function (80–80 [17-OHCS mg./24 hr.] + aetiocholanolone μg./24 hr.), derived from assays of urinary corticosteroids (17-OHCS) and aetiocholanolone, tended to be negative in women with advanced breast cancer who did not benefit from subsequent adrenalectomy or hypophysectomy, and positive in those who did benefit. Further studies showed that, of 39 cases taken in the early stages of the disease, 24 had negative discriminants, whereas in 47 normal women under the age of 80 only 1 had a negative discriminant. Attempts were being made to see if this abnormality preceded the disease by investigation of a large population of normal women.

16. J. B. LOWRY* (R. B. Welbourn), Belfast: "The Effects of 6-Mercaptopurine on Canine Renal Homotransplants".

A total dose of 25 mg. per kg. of 6-MP had been administered in 8 days to test animals and comparisons

made with untreated controls. Treatment of recipient or donor, completed *before* transplantation, had no effect. Treatment started one day before transplantation increased the mean functioning time from 4·7 to 8·3 days and caused leucopenia, lymphoid aplasia, loss of weight, and infection. It reduced the homograft reaction. Removal of the remaining kidney and intravenous injection of homologous marrow 7 days later increased the mean functioning time to 15 days. Death in uræmia occurred while the kidneys were still functioning. A homograft reaction was present. These effects were not great enough to be of clinical value.

17. D. M. HANCOCK* and F. A. MULLAN* (H. W. Rodgers), Belfast: "The Appearance of Hæmagglutinins after Homografts in Rabbits".

Six coloured and 6 albino rabbits were cross-homografted repeatedly in pairs. The albinos received skin-grafts and injections of spleen cells and liver homogenates. The coloured rabbits received skin-grafts only. The hæmagglutinating antibodies which appeared in 3 of the albinos and 4 of the coloured rabbits were explicable by blood group differences between donor and recipient. The reaction in the 5 remaining animals which failed to develop hæmagglutinins could be similarly explained. None of the animals had hæmagglutinins in their sera prior to grafting. There was no relation between the presence or absence of hæmagglutinins and skin-graft survival.

18. H. BURGE, London: "Post-vagotomy Diarrhœa: Its Incidence and its Control by Selective Vagotomy".

19. W. C. WILSON, Aberdeen: "Observations on Serum Antithrombin and the Action of Heparin".

A method of removing 'normal' antithrombin (antithrombin III) from serum had been devised. Antithrombin could be divided into two separate fractions (named here 'X' and 'Y'). The activity of X was enhanced by a brain peptide preparation and by an undefined water-soluble material from a cation exchange resin; by contrast Y was antagonized or suppressed by both. X was destroyed by organic solvents while Y was not affected. The action of heparin was similar to that of peptide and resin material. X is probably the so-called 'co-factor' of heparin.

20. F. M. PARSONS* and C. R. BLAGG* (J. C. Goligher), Leeds: "Diet in Acute Renal Failure".

A rational approach to the dietary management of patients with acute renal failure had been sought. In obstetric cases reduction of the intake of glucose from 100 g. to nil per day doubled the rate of protein catabolism whilst increase of the glucose intake from 100 g. to 200 g. halved the rate. However, norethandrolone (30 mg. per day) had a greater protein sparing activity than 200 g. of glucose. In traumatic cases glucose and norethandrolone had little protein sparing activity. In both groups minimal protein feeding did not increase the rate of protein catabolism.

21. I. D. A. JOHNSTON and R. CHENNEOUR,* Belfast: "The Effect of an Anabolic Steroid on Post-operative Metabolism".

Metabolic balance studies had been performed in 22 patients after operation. Methandienone reduced the mean negative nitrogen balance by 83 per cent ($P<0.01$) in the 5 days after herniorrhaphy (50 mg. per day intramuscularly during the balance period) but not in the 7 days after vagotomy plus gastro-enterostomy (50 mg. per day for 1 week before operation and during the balance period). It augmented the retention of sodium and caused a retention of potassium after herniorrhaphy but not after vagotomy and gastro-enterostomy. Methandienone did not influence the post-operative rise in plasma cortisol or the increase in urinary 17-keto- or 17-ketogenic steroids. In the treated herniorrhaphy group and in *all* the vagotomy plus gastro-enterostomy patients there was a relative reduction in the post-operative rise of 11-keto-aetiocholanolone ($P<0.01$) and 11-hydroxy-aetiocholanolone ($P<0.05$) compared with that of 11-hydroxy-androsterone, and of tetrahydrocortisone compared with tetrahydrocortisol ($P<0.05$). These findings suggest that methandienone does not influence the adrenocortical response to trauma, but that it alters the metabolism of cortisol after mild stress.

22. N. E. WINSTONE,* P. A. SAMPSON,* and B. N. BROOKE, Birmingham: "Adrenocortical Function in Surgical Patients after Steroid Therapy".

The steroid response to operative trauma after steroid therapy had been investigated. The ACTH infusion test had been used pre-operatively in patients with ulcerative colitis, and free 17-hydroxycorticosteroids in the plasma estimated. Operative samples had also been collected for comparison of the ACTH test levels with those produced during surgical stress. All the control patients responded to ACTH, while 3 out of 15 of those previously treated with steroids showed no response. Operative samples indicated that the ACTH infusion test simulated the endogenous stimulus of surgical stress. It was hoped that criteria might be derived for calculation of the minimal corticoid cover for surgery.

23. L. H. STEVENS* and A. W. WILKINSON, Institute of Child Health, London: "Metabolic Response to Injury in the Neonatal Period".

Over 50 newborn children submitted to emergency operation for abnormalities of the alimentary tract had been studied by metabolic balances. A comparison had been made between those who had been treated with various types of intravenous fluid and others who had not received such supplements. Some indications were obtained of the actual daily requirements of newborn children for sodium, potassium, and water during the week which follows a major operation. Variations were observed in the metabolic behaviour of the newborn child after operation compared with that of normal babies of similar age who were not submitted to operation. The nature of some of the alterations and the homeostatic implications were discussed.

24. I. F. MCNEILL,* I. A. PORTER,* and C. A. GREEN* (A. G. R. Lowdon), Newcastle: "Staphylococcal Infection in a Surgical Ward".

A retrospective survey of the records of a general male surgical ward had confirmed the clinical impression of the staff that there had been a fairly high incidence of staphylococcal infection during the preceding 18 months. A 3-month prospective study of this ward had been made to ascertain more accurately the overall incidence of sepsis, the frequency and consequences of staphylococcal infection, and the reasons for the suspected prevalence of this infection. The importance and frequency of staphylococcal infection were confirmed. The major sources of staphylococci were the infected patient and the established nasal carrier who was a danger both to himself and to other patients. The importance of nasal carriage as a source of contamination of the patients' immediate environment and as a source of wound infection was demonstrated.

25. I. F. MACLAREN,* A. R. ISAAC,* B. M. NOLAN,* and A. I. S. MACPHERSON, Edinburgh: "Surgical Infections in Out-patients".

The bacteriological findings in the surgical infections treated by a large casualty department from 1955 to 1960

had been reviewed with the following results: (1) the predominating organism was the *Staphylococcus aureus* pyogenes; (2) the antibiotic-sensitivity pattern of out-patient staphylococcal infection showed no major fluctuation during the period; (3) the incidence of staphylococcal infections sensitive to tetracycline had increased recently; (4) nearly all out-patient staphylococcal infections remained sensitive to chloramphenicol; (5) in the last year the sensitivity rate of staphylococcal infections in out-patients to sulphonamides was at least as high as the penicillin sensitivity rate. A comparison was made between the infections occurring in surgical out-patients and in a general surgical ward.

26. R. K. CARRUTHERS,* J. STEWART,* and D. M. DOUGLAS, Dundee: "The Effect of Theatre Usage on Wound Sepsis in Clean Cases".

The relationship between the placing of cases on operation lists and the rate of subsequent wound sepsis had been investigated. Sepsis was defined as the appearance of pus in the wound at some point in the post-operative period. In 1500 cases of all types the overall sepsis rate was 9 per cent. In clean cases it was 2 per cent, in potentially infected cases 10 per cent, and in emergency cases 15 per cent. In the clean cases those placed first on the operating lists showed a lower incidence of sepsis than later cases ($P<0.05$). Of 550 clean cases, 238 were first on the list and only 1 of these wounds became septic. Of 312 equally clean cases operated on later in the lists, 9 became septic. If the trend continues in further studies, it could have an important bearing on theatre usage and design.

27. G. W. TAYLOR, R. A. SHOOTER,* W. FIELDER,* and P. H. FRANDSEN,* St. Bartholomew's Hospital: "Experimental Staphylococcal Infection".

Standard wounds in the lumbar region of guinea-pigs had been inoculated with varying numbers of a single strain of *Staphylococcus aureus*. Fifty bacteria caused infection of some wounds and 500 caused infection of all. Thread sutures had been freshly inoculated with staphylococci, dried for varying periods, and inserted through the subcutaneous tissue. Drying for 4 hours did not alter the infection rate but 24 hours' drying reduced the sepsis by 60 per cent. The effect of drying was nullified if the threads were originally inoculated with a much larger number of bacteria. This suggests that drying causes bacterial death rather than a reduction in virulence. The infection rate from sutures of different materials and known numbers of bacteria had been compared. The highest incidence of infection occurred with stainless steel.

REVIEWS AND NOTICES OF BOOKS

Petite Chirurgie et Technique Médicale Courante. By G. ROUX and G. MARCHAL. 9½ × 6½ in. Pp. 661 + vi, with 394 illustrations. 1961. Paris: Masson et Cie. 45 NF.

THIS book is intended for students and practitioners. Its scope is wider than its title indicates, ranging from the design and structure of operating theatres to the resuscitation of the apparently drowned, and dealing *en passant* with such subjects as anæsthesia, post-operative treatment, fractures, etc. A large section deals with medical manœuvres such as lumbar and cisternal puncture, paracentesis, etc., and the collection of laboratory specimens.

Minor surgery proper occupies only the last quarter of the book and this section includes ophthalmology, ear, nose, and throat, gynæcology, and urology, as well as general surgery.

The recommended method of securing an indwelling catheter is interesting. Lengths of 'darning cotton' (obtainable, as it says, "in the humblest cottage") are used to fix the catheter to tufts of pubic hair, which are first selected and twisted like the ends of a moustache!

A book of this sort should be a useful introduction and guide to the student and hospital resident. This one fails chiefly in that it is imbued with the teaching and outlook of fifty years ago. The first edition appeared in 1917, during the first world war. It is claimed that the present edition has been brought up to date, but it still carries far too much dead wood. There are descriptions of dry cupping, the use of leeches, and the Paquelin cautery. Pulp infections of the finger are treated by a cruciate incision of the palmar surface. Antibiotics are barely mentioned.

Strangulation Obstruction. By ISIDORE COHN, jun., M.D., D.Sc. (Med.). 9½ × 6½ in. Pp. 273 + xxii, with 90 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications Ltd.). 94s.

THIS book contains the author's experimentation of intestinal obstruction in dogs and his experience in clinical cases of obstruction in human beings. Professor Cohn has reviewed the extensive literature of intestinal strangulation, and has stressed the value of certain tests—such as spectrophotometry. His studies reveal that bacteria undoubtedly are a major cause of death in strangulation obstruction, and that with adequate antibiotic protection fatal cases can be averted.

Every aspect of intestinal strangulation has been covered in this book and many clinical cases are reviewed.

An excellent reference volume, not only for the practical surgeon but also for the experimental surgeon who may have ideas for further research into this problem.

La Radiculographie Lombo-Sacrée par Substance Iodée Hydrosoluble et Résorbable. By JACQUES FERRAND, JEAN ROBERT D'ESLOUGUES, and JACQUES BASSOTTI. 10 × 8½ in. Pp. 108, with 82 illustrations. 1961. Paris: L'Expansion Editeur. No price given.

THIS monograph is based upon the authors' experience of 300 radiological examinations, carried out since 1956, of the lumbar and sacral portions of the cauda equina outlined by the intrathecal injection of methiodal (Kontrast N, Abrodil, Skiodan), a water-soluble, reabsorbable, contrast medium. This is a safe procedure provided the medium remains below the level of the conus medullaris, but it is not suitable for myelography. The injection is preceded by premedication and light spinal analgesia (muscular paralysis is not required) and a series of plates is then exposed with the patient carefully positioned. Contrast appears to be less dense than that obtained with the oily media generally used in this country, and this is probably the reason why screening is not carried out. In other ways the lighter shadow is an advantage, however, as the individual roots of the cauda are separately delineated with wonderful clarity, and indentations and irregularities of their course are clearly seen. In the authors' hands this method proves to be a diagnostic tool of great precision: of 98 patients with

sciatic pain who were submitted to operation, the operative and radiological findings agreed completely in 91, and of these, 3 who had no radiological abnormality had negative operative findings also. Of 80 examinations for lumbago, disk herniæ were detected in 34, and, of these, 15 were operated upon with confirmatory findings.

Although bound as a paper-back, the book is beautifully produced on glossy paper, and the radiographs and accompanying line drawings are of a very high standard. It will undoubtedly be of interest and value to all interested in the radiological diagnosis or treatment of lesions of this part of the spinal canal. A list of about 200 references concludes the work.

Prosthetic Valves for Cardiac Surgery. Edited by K. ALVIN MERENDINO, M.D. 9 × 6 in. Pp. 586 + xxix, with 383 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications Ltd.). 66s.

THIS book contains the various papers which were presented at a Conference on Prosthetic Valves for Cardiac Surgery held in Chicago in September, 1960.

The advance in cardiac surgery since the war has been phenomenal and in the United States no less than 51 research groups are working on valve prosthesis.

This large volume contains a vast amount of useful material on every aspect of valve prostheses. Besides this, the physical aspect of valve function and the hydraulics of blood-flow through the valves are presented.

The various operative techniques and total valve replacement are given in detail.

The book also contains the clinical experiences of many surgeons.

As a reference volume on this subject the book could not be bettered.

La Radiculographie Lombaire dans la Sciatique. By J. ECOIFFIER. 10 × 6½ in. Pp. 140, with 88 illustrations. 1960. Paris: Masson et Cie. 40 NF.

THE radiographic examination of the lumbosacral canal and its contained nerve-roots by the intrathecal injection of methiodal has been practised by the author of this book on more than 700 occasions during the past six years, and he describes the fruits of this experience in the present work, the first monograph to appear on the subject in France.

His methods and findings are similar to those of the subsequent work by Ferrand, D'Eslougues, and Bassotti, reviewed above, though the plan of the book is somewhat different, more space being devoted to discussion of the theoretical basis, techniques, and complications, and less to the tabulation of cases and the analysis of results. The second half of the book is an annotated atlas of radiographs with accompanying drawings, illustrating normal and abnormal findings. All those who investigate or treat sciatic pain will be interested by this and the subsequent work.

Die Chirurgie des Magensarkoms. By A. GÜTGEMANN and H. W. SCHREIBER. 9½ × 6½ in. Pp. 95, with 31 illustrations. 1961. Stuttgart: Georg Thieme. DM. 28.50.

SARCOMA of the stomach is ably and extensively discussed in this well-produced and concise monograph. As few individual medical men meet a large number of cases it is good to have at hand a review in which the present state of our knowledge is summed up. Strangely enough, the prognosis of gastric sarcoma is better than that of carcinoma, as subtotal radical resection offers a better chance for cure. Especially in a case of malignant gastric tumour of dubious resectability it is important that the surgeon should be aware of the possibility of a sarcoma being present, before rejecting an attempt at radical operation. A clear description of the surgical pathology—which is perhaps the most helpful section of this book—is followed by a summing up of the clinical features, including radiographic signs and differential diagnosis. Finally treatment, both radical and palliative, is outlined. Anyone likely to come across cases of gastric sarcoma would be well advised to read this little book.

Histoire de la Chirurgie. By CLAUDE D'ALLAINES. 7 × 4 in. Pp. 128. 1961. Paris: Presses Universitaires de France. No price given.

WITHIN a limited compass this work deals with the development of surgery from ancient times to the present day. Appearing in a popular series of paper-backs entitled *Que sais-je?* it is suited both to the lay public without special knowledge of surgery, and to the surgeons without specialized knowledge of history. For both these groups it provides an admirably balanced account of its subject.

A Radiographic Index. By MYER GOLDMAN, M.B., Ch.B., D.M.R.D., RONALD S. MILLER, M.R.C.S., L.R.C.P., D.M.R.D., and DAVID COPE, F.S.R. 6¼ × 4 in. Pp. 80 + viii. 1961. Bristol: John Wright & Sons Ltd. 13s. 6d.

THIS is a very practical and useful pocket book which should prove invaluable to radiographers and nurses who are working in the X-ray department of any hospital. Medical students will also find much to interest them on how various examinations—such as barium meals and pylograms—are carried out.

A very useful appendix on the various contrast media is included, the common or approved names being given alongside the proprietary name.

A very serviceable glossary of medical terms is also given.

The authors have certainly put the present and future generations of radiography students in their debt.

Die Erkrankungen der Gallenwege und des Pankreas. By WALTER HESS. 10 × 6¾ in. Pp. 672, with 267 illustrations. 1961. Stuttgart: Georg Thieme. DM. 142.

WHENEVER any branch of surgery has undergone radical changes there comes a time when the recent progress should be summed up and made available to those who have not been taking an active part in bringing it about. 'Diseases of biliary tract and of the pancreas' by Walter Hess fulfils this need.

As the author states in his introduction, hardly any really new operations on the biliary tract have been introduced during the last 40 years. However, our knowledge of the pertinent surgical physiology has made such rapid progress lately that it becomes necessary to revise completely our intra-operative diagnosis and strategy. As the advances made were mainly due to the introduction of radiomanometry, it is understandable that the main part of this book is devoted to these procedures and their operative consequences. Those who are intending to introduce these methods into their clinics, or have recently started doing so, will find in this magnificent book the reasons for and the radiographic proof of their faith in them.

The general arrangement is very refreshing. We do not find the usual subdivision into separate diseases, which are further split up into aetiology, signs and symptoms, pathology, etc. Instead the different sections cover the whole field, so that, for example, that on operative technique describes all operations, that on diagnosis discusses all the symptoms and signs, etc.

There are nine sections: anatomy; physiology; pathology with signs and symptoms; diagnosis, including that during operation; operative technique; choice of

operations; anæsthesia; post-operative treatment; 'post-cholecystectomy syndrome'. Each section is followed by a reasonably complete and up-to-date list of references. The cholangiographs are of a high order and well produced, forming an atlas to guide not only the beginner.

The present volume is the outcome of many years' devotion to the practice and study of biliary tract and pancreatic surgery. It incorporates the author's personal experience and the results of Nissen's Surgical Department at Basel, amounting to about 1600 operations together.

Dr. Hess's main ambition has been to write a practical guide for surgeons and radiologists. He has succeeded very well. The usefulness of his book is not confined to radiomanometry alone. It covers in a very comprehensive manner the whole field of surgery of the biliary tract and pancreas in its broadest sense. It is probably the best single available book, worth studying and worth having, despite its high price.

Drugs in the Treatment of Disease. From the *British Medical Journal*. 8½ × 5½ in. Pp. 516 + x. 1961. London: British Medical Association. 35s.

THIS volume consists of a series of specially commissioned articles from the *British Medical Journal*. The authors compare the efficacy of different drugs, give recommendations on dosage, and discuss toxic effects.

All the articles are good and are written by experts in their own particular subject. Sedatives, hypnotics, analgesics, antihistamines, diuretics, and corticosteroids are but a few of the subjects considered. An excellent index is included in the book. Just the volume for the senior student and the busy practitioner.

Frontiers of Mammary Cancer. By CHARLES HUGGINS, M.D., M.Sc., Yale, D.Sc., Acadia Professor of Surgery in the University of Chicago. 8 × 5½ in. Pp. 32. 1961. Glasgow: Jackson, Son & Co. 7s. 6d.

THIS small monograph contains the tenth Macewen Memorial Lecture delivered in the University of Glasgow on June 26, 1958.

No one is better fitted to deliver this important lecture than Charles Huggins, of Chicago, for his researches into mammary cancer are known the world over.

In a concise well-worded lecture he has given an excellent survey of the present position of cancer research, particularly concerning mammary cancer.

Some Aspects of Obliterative Vascular Disease of the Lower Limb. By J. A. GILLESPIE, M.D., Ch.M., F.R.C.S., and D. M. DOUGLAS, Ch.M., F.R.C.S. 9½ × 6¾ in. Pp. 136 + vii, with 68 illustrations. 1961. Edinburgh: E. & S. Livingstone Ltd. 30s.

THIS monograph has appeared at an opportune time, when the medical profession as a whole are seeing more and more cases of obliterative vascular disease, because people are living longer.

On reading through this book the first thing that strikes one is the excellence of the illustrations, especially the photomicrographs, which are superb.

The authors, with their matured clinical background, are able to bring out the salient points in the treatment of this all too common condition, and their assessment of the use of vasodilator drugs and lumbar sympathectomy is of great interest. It is time that someone came into the open and stated that vasodilator drugs are of no value in the treatment of obliterative vascular disease of the lower limb. The authors also state that "The response to oral or intravenous vasodilators gives no indication of the likely response to sympathectomy, and such tests should be abandoned."

The question of lumbar sympathectomy is debated in an able way, and in the majority of cases its place is now being taken by vascular grafting.

The chapter on direct arterial surgery is excellent, and the authors have described their operative technique in a very lucid way.

This book is ideal for the senior student and for the practitioner who wishes to know what is the best treatment for obliterative vascular disease of the lower limb. An excellent monograph.

A Short History of Clinical Pathology. By W. D. FOSTER, M.D. 8¾ × 6½ in. Pp. 154 + xii, with 32 illustrations. 1961. Edinburgh: E. & S. Livingstone Ltd. 27s. 6d.

THIS small volume contains a wealth of information and is written in a clear and concise style. The origin of any medical society or branch of medicine is always of interest to the medical historian, and it is curious to find that several clinical pathologists were historians.

It is pleasing to note that Dr. Foster has included the portrait of Sir William Watson-Cheyne in his book, and it is stimulating to read about the early career of this one-time President of the Royal College of Surgeons of England. Foster writes: "In the early 1880's, Cheyne was probably the best bacteriologist in Great Britain." It should be noted that Cheyne was appointed Assistant Surgeon to King's College Hospital in 1880 and thereafter he was busy with surgery.

The history of clinical pathology starts with morbid anatomy and histology, and passes through periods in which clinical microscopy, chemical pathology, clinical bacteriology, and diagnostic serology came into being.

Some excellent photographs are to be found in this book, and we are pleased to see that those of S. C. Dyke, Cuthbert Dukes, W. H. McMenemey, and Sir Philip Panton are included.

A good account of the Association of Clinical Pathologists, which was founded in 1924, is given.

This book should interest all clinicians and historians as well as the pathologists at home and abroad. The price of the book is most moderate.

Treatment of Cancer and Allied Diseases. Vol. 4: Chest and Esophagus. By G. T. PACK, M.D., F.A.C.S., and I. M. ARIEL, M.D., F.A.C.S. 10 × 6½ in. Pp. 667 + xix. Illustrated. 1961. London: Pitman Medical Publishing Co. Ltd. £12.

THE second edition of the fourth volume of this comprehensive work, devoted to the treatment of cancer of the breast, chest, and œsophagus, is very authoritative, for there are no less than sixty-seven contributors. All these persons deal with some aspect of cancer occurring in breast or thorax.

Every variety of technique is given and illustrated, and the pre- and post-operation treatments are well described. Modern radiotherapy, the use of hormones, and chemotherapy are all explained in detail. This will be the book of reference for many years to come.

Recurrent Dislocation of the Shoulder. By H. F. MOSELEY, M.A., D.M., M.Ch. (Oxon.), F.R.C.S. (Eng. & Canada), F.A.C.S. 10¾ × 8½ in. Pp. 163 + xii, with 128 illustrations. 1961. Edinburgh: E. & S. Livingstone Ltd. £6.

THIS is a large comprehensive volume dealing with every aspect of recurrent dislocation of the shoulder and its treatment.

The author has made a special study of the shoulder-joint and the various dislocations which may take place there, and the present volume presents his experience and operative technique. The illustrations, many of which are in colour, are excellent, and do help the reader to appreciate the text.

Few surgeons can have operated upon 125 cases of recurrent dislocation of the shoulder, and yet Moseley gives his series since 1938 and their follow-up.

A unique feature of this volume is the inclusion in a back pocket of a compact stereoscopic viewer, and five viewmaster stereoscopic reels containing 35 colour photographs of the lesions produced by recurrent dislocation of the shoulder.

Included in this volume is a formidable list of 1051 references dealing with this type of dislocation. As a reference volume it could not be bettered.

Traumatic Lesions of Peripheral Vessels. By C. W. HUGHES, A.B., M.D., and W. F. BOWERS, A.B., B.Sc., M.D., M.S., Ph.D. 9 × 6 in. Pp. 197 + x, with 58 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications Ltd.). 64s.

IN this traumatic age this book appears at an opportune moment, when injury to the peripheral vessels is all too common both at home and abroad. The time has come for a reassessment of these injuries and to consider in detail how they are to be treated.

This book gives the answers to many important problems in traumatic injuries to the various peripheral vessels. An excellent account is given of the various prosthetic devices which have been used to bridge vascular defects. The illustrations throughout the book are of a high order, and the text is written in a direct and lucid style.

A good bibliography of some 443 references is included, which will be found most useful to those surgeons who may wish to increase their knowledge in this all too important subject.

Surgical Diseases of the Lung. By BUFORD H. BURCH, M.A., M.D., and ARTHUR C. MILLER, M.S., M.D., F.A.C.S. 9½ × 6 in. Pp. 128 + xii, with 60 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications Ltd.). 68s.

THIS is a unique book in many ways, for it is devoid of bibliography, references, and an index. Yet it is a most informative monograph because it contains the views and experience of two matured clinicians who have studied their subject very thoroughly.

The surgical treatment of lung diseases has advanced at a great rate over the last two decades. There are many factors which have been responsible for this advance, the most important being: modern anæsthesia, penicillin and the antibiotics, and the use of blood transfusion. These factors have enabled the thoracic surgeon to make a bold exposure of the lung.

Doctors Burch and Miller have written a stimulating book, full of useful practical information. An excellent collection of good radiographs is given at the end of the book, and this will be most helpful to the reader for they do present the facts far more clearly than an extension of the text.

Modern Surgery for Nurses. Edited by F. WILSON HARLOW, M.B., B.S. (Dunelm.), F.R.C.S. (Eng.), Fellow of the International College of Surgeons; Associate Member British Association of Urological Surgeons (Home and Overseas); Emeritus Consultant Surgeon, Wessex Regional Hospital Board. Fifth edition. 8½ × 5½ in. Pp. 883 + xxiv, with 419 illustrations. 1961. London: William Heinemann (Medical Books) Ltd. 30s.

THE usefulness and popularity of this book can be judged by the fact that the first edition appeared in 1948, and many reprinted editions have been necessary in addition to the four editions themselves. These facts speak for themselves and the editor is to be congratulated on this new fifth edition; also on the wise manner in which he has selected his contributors. The whole extensive field of modern surgery has been covered in a very able and simple fashion so that all nurses can understand the text.

The illustrations are well chosen and clear; there is not a poor illustration in the whole book.

The price of the book is most moderate; and every nurse should possess a copy.

The Extraction of Teeth. By GEOFFREY L. HOWE, M.R.C.S., L.R.C.P., F.D.S. 8¾ × 5½ in. Pp. 80 + vii, with 100 illustrations. 1961. Bristol: John Wright & Sons Ltd. 17s. 6d.

THIS is a very sound, practical book which should prove of real value not only to students, but also to practitioners. Although practical experience is the thing that matters in extraction of teeth, yet by reading through this book the student will gain a lot of knowledge which will be most useful to him.

The illustrations throughout the book are excellent and many of them are original. The black-and-white drawings are very hard to beat and they have the great advantage of being simple.

We agree with Sir William Kelsey Fry, who writes a foreword to this book, when he states that "The author has done a valuable service to both undergraduates and post-graduates in pointing out the need to understand the basic principles underlying the techniques for the removal of individual teeth."

An excellent little monograph.

The Surgical Treatment of Intracranial Meningiomas. By COLLIN S. MACCARTY, B.A., M.D., M.S. 9 × 6 in. Pp. 69 + viii, with 15 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications Ltd.). 36s.

THIS monograph is based on the author's extensive experience at the Mayo Clinic. The total experience of the Mayo Clinic with meningiomas since 1914 is considerably in excess of 1000 cases. When it is considered that this form of tumour of the brain has an incidence of between 13·4 and 19·4 per cent among all tumours of the brain, one can understand the large number of tumours which come to the Mayo Clinic for treatment each year.

The author, in this book, has devoted himself to the surgical treatment of meningiomas, and he has written a very interesting and very practical volume. The illustrations throughout the book are original and do in a large measure enhance the value of the written word.

A very comprehensive list of references is given at the end of the book.

The neurologist and the neurosurgeon will find much to interest them in this excellent monograph.

Tools of Biological Research. Edited by HEDLEY J. B. ATKINS, D.M., M.Ch. (Oxon.), F.R.C.S. (Eng.), Hon. F.A.C.S., Director of the Department of Surgery, Guy's Hospital. Second series. 8¾ × 5½ in. Pp. 175 + xii, illustrated. 1960. Oxford: Blackwell Scientific Publications Ltd. 37s. 6d.

THIS book covers the papers which were read at the second Symposium of this type held in October, 1959, at Guy's Hospital, London. On this occasion a completely new series of techniques employed by research workers was brought to the notice of surgeons, some of these techniques already having found their way into routine practice in the investigation of patients. The introduction is by Lord Cohen of Birkenhead. The ten contributions are all written by experts, and there is some variation, partly in the nature of the subjects, in the way in which they have been described in terms which the clinician can follow without specialized knowledge. However, here he will be able to turn in order to learn something of the basic science and the methods on which these investigations depend, and the references at the end of each chapter show where further information may be found. Of particular interest to surgeons are the chapters

on electro-encephalography, paper chromatography, and microradiography. Other subjects of clinical application are the ultracentrifuge, fluorescent antibody techniques, phonocardiography, vector cardiography, and the application of the cathode-ray oscillograph to electromyography. Of interest mainly to specialized research workers are the chapters on electron spin resonance spectroscopy and X-ray diffraction studies.

Those who were privileged to attend this symposium will appreciate the opportunity of studying these lectures in detail, and the book will be a source of reference regarding these technical procedures.

A Doctor's Memoirs. By A. J. WILLINSKY. 8¾ × 5½ in. Pp. 183. 1961. London: Macmillan & Co. Ltd. 28s.

THE life history of a doctor often makes interesting reading, and especially so if the doctor happens to be a surgeon who has travelled widely.

The autobiography of Dr. A. I. Willinsky covers an interesting period in the history of surgery, for he saw the antiseptic routine followed by the aseptic technique. He probably saw the development of Canadian surgery, and the special branch of urology better than any other medical man.

Although a Jew, Dr. Willinsky has once again proved that it matters little what creed a man belongs to, for if he has the energy and perseverance he will win through.

This book is written in a lively style with innumerable human stories which only a doctor can tell. It is a book that once the reader starts to read he cannot put down until he has finished it. This surely is true praise.

Surgery of the Aorta and its Branches. By JAMES D. HARDY, M.S. (Chem.), M.D., F.A.C.S. 7½ × 4½ in. Pp. 386 + xiv, with 75 illustrations. 1961. Philadelphia and Montreal: J. B. Lippincott Co. (London: Pitman Medical Publishing Co. Ltd.). 52s.

THIS is a useful little monograph dealing with the various operations that may be performed on the aorta and its branches. The many and varied grafting operations that are in use at the present time are well described and illustrated.

To-day, arterial embolism constitutes a serious clinical problem, and Professor Hardy, with his extensive and mature clinical background, is at his best when discussing the treatment of arterial embolism.

Traumatic injuries of the aorta and the large vessels receive adequate attention, and the operative techniques are considered in a very practical way.

An excellent small monograph.

Medicine and the Navy, 1200–1900. Volume 3, 1714–1815. By CHRISTOPHER LLOYD, F.R.Hist.S., Assistant Professor, Royal Naval College, Greenwich, and JACK L. S. COULTER, F.R.C.S., Surgeon Captain, Royal Naval Medical School. Pp. 402 + xi. 1961. Edinburgh and London: E. & S. Livingstone Ltd. 50s. net.

THE publication of the third volume of this important work will be welcomed by the medical profession as a whole. The untimely death of Surgeon Commander John Keevil was a great shock to his many friends, and it was a major loss to the history of medicine for he never saw the second volume of *Medicine and the Navy*. It is quite right and proper that the editors of the third volume should dedicate it to John Keevil.

The Wellcome Trustees are to be congratulated on their choice of editors for this third volume, for it is in every way a very worthy successor to the two previous volumes.

Mr. Christopher Lloyd is Assistant Professor of History and English at the Royal Naval College, Greenwich, and is steeped in Naval History, and Surgeon Captain Coulter has had considerable experience in recording the Medical History of World War 2. The happy combination of these two authors has resulted in an excellent book full of interesting and historical data. They have a fascinating story to tell and they tell it well. The status of the Surgeon in the Navy is given in true perspective, and one wonders why these medical men ever joined the Navy, for their conditions of service were terrible.

During the years 1714–1815 the medical history of the Navy is closely associated with the City of London and the Barber-Surgeons' Company. The Surgeons' Company and the Society of Apothecaries are well represented in this third volume.

The illustrations throughout the book are excellent and have been well chosen.

This volume, like the former volumes, should be in every library and in every Medical School, for it will long remain the reference volume on this important subject.

Surgery of the Esophagus. By RAYMOND W. POSTLETHWAIT, B.S., M.D., and WILL CAMP SEALY, B.S., M.D. 11 × 8½ in. Pp. 482 + xiv, with 201 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications Ltd.). £12.

THIS large volume, of nearly five hundred pages, gives a very practical and comprehensive account of the surgery of the œsophagus as seen at the Duke Medical Centre since its opening over thirty years ago.

The various operative techniques for cancer of the œsophagus are well described and illustrated.

The anatomy and physiology of the œsophagus are set forth in an interesting and quite original way. At the end of each of the fourteen chapters which go to make up this volume there is an extensive list of references.

This book gives a comprehensive picture of current concepts of œsophageal disease. As a reference volume it could not be bettered.

Neuroradiology Workshop. By LEO M. DAVIDOFF, M.D., HAROLD G. JACOBSON, M.D., and HARRY M. ZIMMERMANN, M.D. 11 × 8 in. Pp. 256, with 89 illustrations. 1961. New York and London: Grune & Stratton Ltd. $16.50.

THIS is a unique book in many ways, for its title does not inform the reader regarding its contents. The book is divided into four large chapters:—

The first chapter, by way of introduction, deals with the development of neuroradiology and the use of pneumoencephalography and cerebral angiography.

Chapter II is concerned with craniocerebral tumours and the classification of 271 cases seen at the Montefiore Hospital, the three commonest being gliomas, pituitary tumours, and meningiomas.

Chapter III includes tumours of the scalp and skull, and some 14 clinical cases are described, the radiographs of the skull being presented in each case. A useful comment is given at the end of the clinical and operative findings.

Chapter IV, by far the largest in the book, deals with the meningiomas and contains the clinical history, radiographs, and operative findings of 42 cases. The X-ray pictures are very fine and beautifully reproduced.

This is a novel way of presenting neurosurgical material that has been investigated to the full.

The book should prove a useful reference volume.

Injuries and Infections of the Hand. By ROBERT H. C. ROBINS, M.A., M.B., B.Chir., F.R.C.S. 9¾ × 7¼ in. Pp. 220 + xii, with 157 illustrations. 1961. London: Edward Arnold (Publishers) Ltd. 63s.

IN these modern times with the ever-increasing amount of trauma produced on the roads of the world, it is fitting that yet another book on injuries and infections of the hand should be published.

In reality, this monograph is an expansion of Mr. Robins' essay on "The treatment and preservation of the injured hand", which in 1952 won him the first James Berry prize of the Royal College of Surgeons of England.

For over ten years the author has been interested in, and treating, injuries of the hand, and has collected a vast amount of material which he has analysed in this book.

As one would imagine, no book on injuries and infections of the hand would be complete without adequate pictures to illustrate and enhance the value of the text. In this monograph there are over 150 illustrations, all of good quality, and some in colour.

There are many new techniques which have been involved in the treatment of injured fingers, and the author has incorporated the best of these in his book.

A very useful book. It is to be hoped that many casualty officers—both at home and abroad—will read it.

La Laparoscopie. By G. LENZI, G. B. CAVASSINI, and E. LENZI, in two volumes. I, Text with 344 pages, 55 figs.; II, Atlas with 126 pages, 56 colour plates. 1961. Paris: Masson et Cie. 100 NF.

LAPAROSCOPY, or 'peritoneoscopy' as we more often term it, is rather rarely employed in this country; it has always been more popular on the Continent and there it appears to be growing in its importance and in its breadth of application. Modern instruments enable colour photographs of great clarity to be taken for permanent record; biopsy specimens, particularly of liver, to be obtained under direct vision; and even cholangiography to be performed by puncture of the gall-bladder.

This publication, translated from Italian into French, is from the clinic of Professor Sotgiu of Bologna; it is based on an experience of over 1000 laparoscopies. The first volume gives a full review of the technique, indications, and complications of this examination, followed by an account of the normal and abnormal appearances which may be obtained. The second volume is a beautifully produced colour atlas which illustrates both normal and abnormal appearances, together with a selection of typical biopsy specimens. There is a full bibliography.

Surgery is Destined to the Practice of Medicine. By Sir REGINALD WATSON-JONES, B.Sc., M.Ch.Orth., F.R.C.S., F.R.A.C.S. (Hon.), F.R.C.S.E. (Hon.), F.A.C.S. (Hon.), Orthopædic Surgeon-Extra to Her Majesty the Queen, Orthopædic Surgeon to His Late Majesty King George VI. 10 × 6¾ in. Pp. 81, with 77 illustrations. 1961. Edinburgh: E. & S. Livingstone Ltd. 21s.

THIS monograph contains the ninetieth Hunterian Oration, delivered at the Royal College of Surgeons of England by Sir Reginald Watson-Jones on February 16, 1959.

He traces the beginning of orthopædic surgery down to the present day and gives several examples of clinical conditions which were seen fifty years ago.

There are some excellent pictures of John Hunter, and some of his furniture. The coloured pictures are excellent and are well reproduced.

A list of Hunterian Orators from 1814 to the present day will prove useful for reference purposes.

This monograph will appeal to all who are devoted to the Hunterian tradition and to Hunteriana.

Les Ictères Post-Opérative Précoces. By F. POILLEUX and A. KAPANDJI. 9 × 7 in. Pp. 108, with 36 illustrations. 1961. Paris: L'Expansion Editeur. 14 NF.

THE occurrence of jaundice after operation is disturbing to the patient and often even more so to the surgeon. In this excellent little book the authors describe the varieties of jaundice which may develop in the first three weeks after operation. A synoptic style, aided by diagrammatic drawings, enables a great deal of ground to be covered in a small space. Both 'surgical' and 'medical' jaundice are dealt with, and diagnosis, prevention, and treatment discussed fully.

As might be expected from French authors, considerable importance is attached to pre-operative cholangiography and manometry. Cirrhosis of the liver would appear to be a common cause of post-operative jaundice in France.

A book to be recommended both to the post-graduate student and the practising surgeon.

Management of Fractures, Dislocations, and Sprains. By H. EARLE CONWELL, M.D., F.A.C.S., and FRED C. REYNOLDS, M.D. Seventh edition. 9¾ × 6 in. Pp. 1153, with 1227 illustrations. 1961. St. Louis: C. V. Mosby Co. (London: Henry Kimpton). £10 2s. 6d.

THIS large and comprehensive work, which was first published in 1934, has remained a popular book on both sides of the Atlantic, and the new seventh edition will still prove a favourite.

Every facet of fracture surgery has been covered in this exhaustive volume, which has more than one illustration to a page. These numerous illustrations have been carefully chosen and are beautifully reproduced.

The chapters dealing with injuries and sprains are excellent.

This book will long remain the reference volume on fractures in this age of trauma.

Tumors of the Female Sex Organs. By ARTHUR T. HERTIG, M.D., and HAZEL GORE, M.B., B.S. 10¼ × 7¾ in. Pp. 176, with 157 illustrations. 1961. Washington, D.C.: Armed Forces Institute of Pathology. $1.40.

THIS excellent atlas of pathology—devoted to the tumours of the ovary and Fallopian tube—is beautifully produced, and contains some of the best photomicrographs that have so far been published.

The authors give a pre-eminent account of the classification of ovarian tumours and stress the clinical manifestations.

This book is Fascicle 33 of the *Atlas of Tumor Pathology*, which is in process of publication by the Armed Forces Institute of Pathology in America. As each fascicle is published the authors seem to produce something finer than the previous volume. There can be no doubt whatsoever that this atlas will become the reference work of the whole medical world.

The Practical Management of Head Injuries. By JOHN M. POTTER, M.A., M.B., B.Chir., F.R.C.S., Consultant Neurosurgeon to the Manchester Royal Infirmary. Pp. 84 + xii. 1961. London: Lloyd-Luke (Medical Books) Ltd. 12s.

THIS is a most useful little monograph packed with important facts. It is small enough to be carried in the pocket, and in this sense will appeal to students and casualty officers.

In this age of trauma, when some 1000 motor-cyclists are killed on the roads each year, the majority of these fatalities are due to head injuries.

Mr. Potter has been at pains to present his book in a clear, readable form.

Brian Elliott has written an excellent appendix entitled "Lost Bouquets", in which he bemoans the loss of smell due to head injury. This convinces the reader that loss of smell is a disability of some magnitude.

Sir James Paterson Ross has written a foreword in which he rightly praises Mr. Potter for writing such an important book.

This book should be read by all students, for it gives them an excellent clinical picture of what is all too often a difficult condition to diagnose, assess, and treat.

Surgical Diseases of the Chest. Edited by BRIAN BLADES, M.D. 9¼ × 6¾ in. Pp. 580, with 267 illustrations. 1961. St. Louis: C. V. Mosby Co. (London: Henry Kimpton). £8 5s.

THIS large volume, devoted to the surgical diseases of the chest, covers the whole aspect of the subject, and is made up of sixteen chapters written by some eighteen contributors.

The subject of thoracic trauma is a large one to-day, and this is very well covered.

The surgical problems of congenital heart disease and acquired heart disease occupy a large part of this work, while the aorta and the great vessels receive due attention. The chapters on the lungs and pleura are, perhaps, the best in the book.

The whole subject of the surgery of the chest is a vast one to-day, and it attracts some of the best of the younger generation of surgeons. This volume will be of real value not only to surgeons who want a good reference volume, but also to registrars and hospital residents who wish to know how to treat surgical diseases of the chest.

Carcinoma of the Colon. By E. G. MUIR, F.R.C.S. 9 × 5½ in. Pp. 181, with 61 illustrations. 1961. London: Edward Arnold (Publishers) Ltd. 42s.

THIS monograph is based on the Lettsomian Lectures which were delivered by the author at the Medical Society of London in 1956, and it is full of useful practical information.

Mr. Muir has written a useful and interesting book, which relates his experience in this branch of surgery, which he has made his own. He has stressed the difficulties which are likely to occur in operations for the relief and cure of colonic cancer.

A matured clinical background is of fundamental importance, and the author has this great asset; also, he has the gift of easy diction and expression.

The illustrations have been well chosen and are beautifully reproduced. The book should prove of real value to the post-graduate, and especially to the surgical registrar who is working for a higher surgical degree or diploma.

The price of this monograph is most moderate.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Thrombosis and Anticoagulant Therapy. Proceedings of a Symposium held in Queen's College, Dundee, Sept. 29–Oct. 1, 1960. Edited by W. WALKER. 9½ × 7 in. Pp. 106. Illustrated. 1961. Edinburgh: E. & S. Livingstone Ltd. 17s. 6d.

Chirurgie des Voies Biliaires. Extra- et Intra-Hépatiques. By CLAUDE OLIVIER. 9½ × 6 in. Pp. 612 + xii, with 255 illustrations. 1961. Paris: Masson et Cie. 100 NF.

Klinische Chirurgie für die Praxis, Vol. I, No. 5. Edited by Prof. Dr. med. O. DIEBOLD, Prof. Dr. med. H. JUNGHANNS, and Prof. Dr. med. L. ZUKSCHWERDT. 10¾ × 7¼ in. Pp. 151 + 18, with 102 illustrations. 1961. Georg Thieme. DM. 39.

Tumeurs de l'Uretère, Abouchements Ectopiques de l'Uretère, les Uretèrocèles. By JEAN CIBERT, G. RIGONDET, and JACQUES CIBERT. 9½ × 6½ in. Pp. 252 + viii, with 63 illustrations. 1961. Paris: Masson et Cie. 52 NF.

Le Kyste Hydatique. By P. GOINARD, J. PEGULLO, and G. PÉLISSIER. 9¾ × 6½ in. Pp. 204, with 90 illustrations. 1961. Paris: Masson et Cie. 45 NF.

Pathologie Chirurgicale des Voies Biliaires Extra-Hépatiques. By MARCEL ROUX, CHARLES DEBRAY, R. LE CANVET, and RENÉ LAUMONIER. 9½ × 6½ in. Pp. 346, with 143 illustrations. 1961. Paris: Masson et Cie. 54 NF.

Human Decisions in Complex Systems. Edited by WARREN S. MCCULLOCH, being Vol. 89, Art. 5 of Annals of the New York Academy of Sciences, Jan. 28, 1961. 9 × 6 in. Pp. 715–896. 1961. New York: New York Academy of Sciences. No price given.

Cerebral Palsy in Childhood and Adolescence. By J. L. HENDERSON, M.D., F.R.C.P.E., Professor of Child Health, University of St. Andrews; Consultant Pædiatrician, Eastern Regional Hospital Board, Scotland. 8½ × 5½ in. Pp. 404. 1961. Edinburgh: E. & S. Livingstone Ltd. 35s.

Die Präoperative Röntgenbestrahlung des Mammakarzinoms. By E. MUNTEAN. 9½ × 6½ in. Pp. 108. Illustrated. 1961. Stuttgart: Georg Thieme. DM. 17.50.

Klinische Chirurgie fur die Praxis. By O. DIEBOLD, H. JUNGHANNS, and L. ZUKSCHWERDT. Volume III, part 3. 10½ × 7 in. Pp. 221, with 80 illustrations. 1961. Stuttgart: Georg Thieme. DM. 41.

Encyclopedia of Urology. Edited by C. E. ACKEN, V. W. DUX, H. M. WEYRACH, and E. WILDBOLZ. In 13 volumes. Vol. I: Operative Urology by W. BISCHOF, P. BISCHOFF, C. FRANKSSON, R. FREY, J. H. HARRISON, J. HELLSTROM, and W. TONNIS. 9½ × 6½ in. Pp. 460 + xii, with 183 illustrations. 1961. Berlin: Springer. Cloth. DM. 176: by Subscription DM. 140.80.

Symposium on Anticoagulant Therapy. Report of the Proceedings. Edited by Professor Sir G. W. PICKERING, M.A., D.Sc., M.D., F.R.C.P. 8½ × 5½ in. Pp. 284 + xii, 78 illustrations. 1961. London: Harvey & Blythe Ltd. 21s.

Einfachheit und Sicherheit bei Magen- und Darmoperationen. By HEINRICH WESTHUES. 11 × 7½ in. Pp. 75 + viii, with 87 illustrations. 1961. Stuttgart: Georg Thieme. DM. 29.

Les Syndromes Abdominaux Aigus Pseudo-Chirurgicaux. By HENRI MERLE. 9½ × 6 in. Pp. 272, with 8 illustrations. 1961. Paris: G. Doin et Cie. 28 NF.

The Spinal Cord. By GEORGE AUSTIN. 9¾ × 6½ in. Pp. 532 + xiii, with 363 illustrations. 1961. Illinois: Charles C. Thomas (Oxford: Blackwell Scientific Publications). £10 12s.

Home Treatment in Injury and Osteo-arthritis. By W. E. Tucker, C.V.O., M.B.E., T.D., M.A., F.R.C.S., Consulting Orthopædic Surgeon, Royal London Homœpathic Hospital. 8¾ × 5½ in. Pp. 80, with 17 illustrations. 1961. Edinburgh: E. & S. Livingstone Ltd. 10s. 6d.

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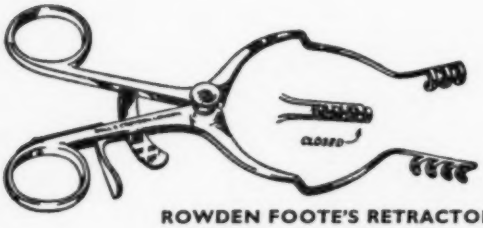

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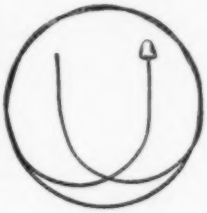

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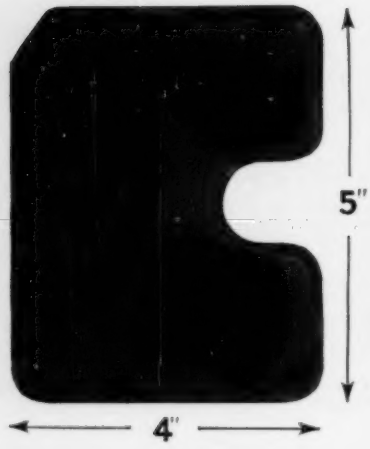

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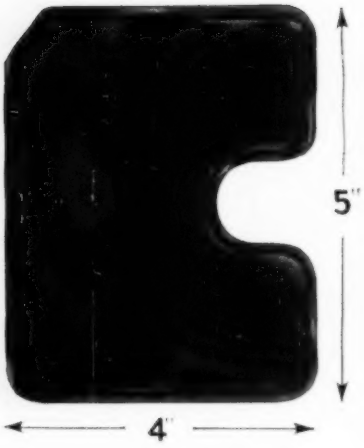

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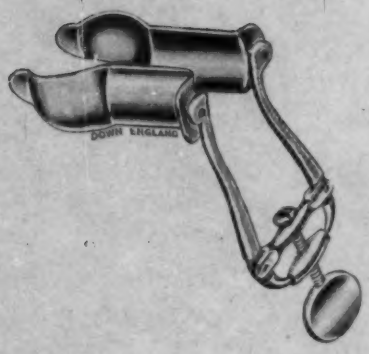

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